

## chain nodes :

4 8 12 13 14 15 16 26 30 31 32 33 34 35 36 37 38 39 40 41 42 43 44  
45 46 47 48 49 50 51 58 59

## ring nodes :

1 2 3 5 6 7 9 10 11 17 18 19 20 21 22 23 24 25 27 28 29 52 53 54 55  
56 57

## chain bonds :

1-34 2-4 6-8 9-13 10-12 13-14 14-15 14-16 22-41 24-33 25-26 27-31 29-30 31-32  
31-59 34-35 35-36 36-37 37-38 38-39 38-40 41-42 42-43 42-44 44-45 45-46 46-47  
47-48 48-49 49-50 50-51 50-52 55-58

## ring bonds :

1-2 1-24 2-3 3-5 5-6 6-7 7-9 9-10 10-11 11-17 17-18 18-19 18-23 19-20 20-21  
20-29 21-22 22-23 24-25 25-27 27-28 28-29 52-53 52-56 53-54 54-55 55-57 56-57

## exact/norm bonds :

1-2 1-24 2-3 2-4 3-5 5-6 6-7 6-8 7-9 9-10 10-11 10-12 11-17 17-18 20-29  
22-41 24-25 25-26 25-27 27-28 28-29 29-30 36-37 37-38 38-39 38-40 41-42 42-43  
48-49 49-50 50-51 55-58

## exact bonds :

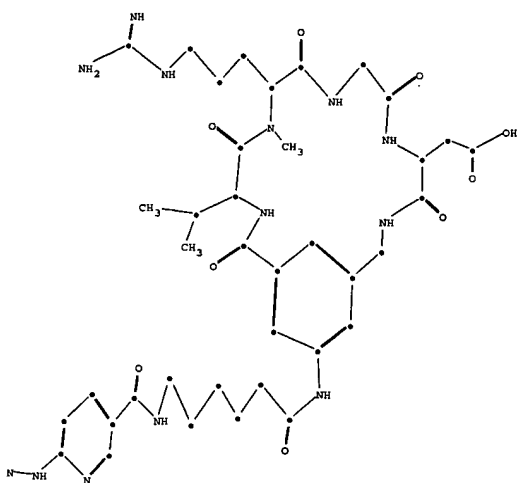
1-34 9-13 13-14 24-33 27-31 31-32 31-59 34-35 35-36 42-44 44-45 45-46 46-47  
47-48 50-52

## normalized bonds :

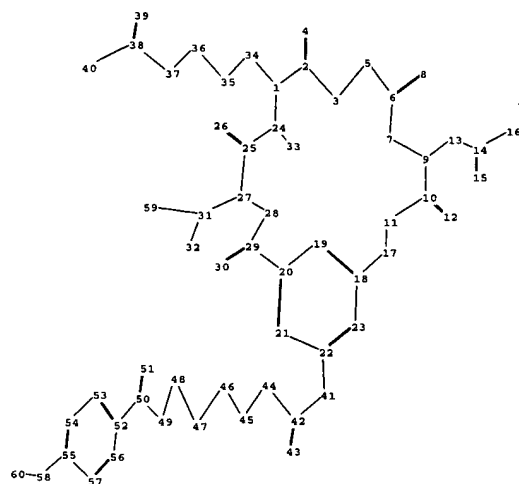
14-15 14-16 18-19 18-23 19-20 20-21 21-22 22-23 52-53 52-56 53-54 54-55 55-57  
56-57

## Match level :

1:Atom 2:Atom 3:Atom 4:CLASS 5:Atom 6:Atom 7:Atom 8:CLASS 9:Atom 10:Atom 11:Atom  
12:CLASS 13:CLASS 14:CLASS 15:CLASS 16:CLASS 17:Atom 18:Atom 19:Atom 20:Atom  
21:Atom 22:Atom 23:Atom 24:Atom 25:Atom 26:CLASS 27:Atom 28:Atom 29:Atom 30:CLASS  
31:CLASS 32:CLASS 33:CLASS 34:CLASS 35:CLASS 36:CLASS 37:CLASS 38:CLASS 39:CLASS  
40:CLASS 41:CLASS 42:CLASS 43:CLASS 44:CLASS 45:CLASS 46:CLASS 47:CLASS 48:CLASS  
49:CLASS 50:CLASS 51:CLASS 52:Atom 53:Atom 54:Atom 55:Atom 56:Atom 57:Atom  
58:CLASS 59:CLASS



14



## chain nodes :

4 8 12 13 14 15 16 26 30 31 32 33 34 35 36 37 38 39 40 41 42 43 44  
45 46 47 48 49 50 51 58 59 60

## ring nodes :

1 2 3 5 6 7 9 10 11 17 18 19 20 21 22 23 24 25 27 28 29 52 53 54 55  
56 57

## chain bonds :

1-34 2-4 6-8 9-13 10-12 13-14 14-15 14-16 22-41 24-33 25-26 27-31 29-30 31-32  
31-59 34-35 35-36 36-37 37-38 38-39 38-40 41-42 42-43 42-44 44-45 45-46 46-47  
47-48 48-49 49-50 50-51 50-52 55-58 58-60

## ring bonds :

1-2 1-24 2-3 3-5 5-6 6-7 7-9 9-10 10-11 11-17 17-18 18-19 18-23 19-20 20-21  
20-29 21-22 22-23 24-25 25-27 27-28 28-29 52-53 52-56 53-54 54-55 55-57 56-57

## exact/norm bonds :

1-2 1-24 2-3 2-4 3-5 5-6 6-7 6-8 7-9 9-10 10-11 10-12 11-17 17-18 20-29  
22-41 24-25 25-26 25-27 27-28 28-29 29-30 36-37 37-38 38-39 38-40 41-42 42-43  
48-49 49-50 50-51 55-58 58-60

## exact bonds :

1-34 9-13 13-14 24-33 27-31 31-32 31-59 34-35 35-36 42-44 44-45 45-46 46-47  
47-48 50-52

## normalized bonds :

14-15 14-16 18-19 18-23 19-20 20-21 21-22 22-23 52-53 52-56 53-54 54-55 55-57  
56-57

## Match level :

1:Atom 2:Atom 3:Atom 4:CLASS 5:Atom 6:Atom 7:Atom 8:CLASS 9:Atom 10:Atom 11:Atom  
12:CLASS 13:CLASS 14:CLASS 15:CLASS 16:CLASS 17:Atom 18:Atom 19:Atom 20:Atom  
21:Atom 22:Atom 23:Atom 24:Atom 25:Atom 26:CLASS 27:Atom 28:Atom 29:Atom 30:CLASS  
31:CLASS 32:CLASS 33:CLASS 34:CLASS 35:CLASS 36:CLASS 37:CLASS 38:CLASS 39:CLASS  
40:CLASS 41:CLASS 42:CLASS 43:CLASS 44:CLASS 45:CLASS 46:CLASS 47:CLASS 48:CLASS  
49:CLASS 50:CLASS 51:CLASS 52:Atom 53:Atom 54:Atom 55:Atom 56:Atom 57:Atom  
58:CLASS 59:CLASS 60:CLASS

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LOGINID:SSSPTA1208DXJ

PASSWORD:

TERMINAL (ENTER 1, 2, 3, OR ?):2

\* \* \* \* \* Welcome to STN International \* \* \* \* \*

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NEWS 3	Apr 09	BEILSTEIN: Reload and Implementation of a New Subject Area
NEWS 4	Apr 09	ZDB will be removed from STN
NEWS 5	Apr 19	US Patent Applications available in IFICDB, IFIPAT, and IFIUDB
NEWS 6	Apr 22	Records from IP.com available in CAPLUS, HCAPLUS, and ZCAPLUS
NEWS 7	Apr 22	BIOSIS Gene Names now available in TOXCENTER
NEWS 8	Apr 22	Federal Research in Progress (FEDRIP) now available
NEWS 9	Jun 03	New e-mail delivery for search results now available
NEWS 10	Jun 10	MEDLINE Reload
NEWS 11	Jun 10	PCTFULL has been reloaded
NEWS 12	Jul 02	FOREGE no longer contains STANDARDS file segment
NEWS 13	Jul 22	USAN to be reloaded July 28, 2002; saved answer sets no longer valid
NEWS 14	Jul 29	Enhanced polymer searching in REGISTRY
NEWS 15	Jul 30	NETFIRST to be removed from STN
NEWS 16	Aug 08	CANCERLIT reload
NEWS 17	Aug 08	PHARMAMarketLetter(PHARMAML) - new on STN
NEWS 18	Aug 08	NTIS has been reloaded and enhanced
NEWS 19	Aug 19	Aquatic Toxicity Information Retrieval (AQUIRE) now available on STN
NEWS 20	Aug 19	IFIPAT, IFICDB, and IFIUDB have been reloaded
NEWS 21	Aug 19	The MEDLINE file segment of TOXCENTER has been reloaded
NEWS 22	Aug 26	Sequence searching in REGISTRY enhanced
NEWS 23	Sep 03	JAPIO has been reloaded and enhanced
NEWS 24	Sep 16	Experimental properties added to the REGISTRY file
NEWS 25	Sep 16	Indexing added to some pre-1967 records in CA/CAPLUS
NEWS 26	Sep 16	CA Section Thesaurus available in CAPLUS and CA
NEWS EXPRESS		February 1 CURRENT WINDOWS VERSION IS V6.0d, CURRENT MACINTOSH VERSION IS V6.0a(ENG) AND V6.0Ja(JP), AND CURRENT DISCOVER FILE IS DATED 05 FEBRUARY 2002
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=> fil reg

COST IN U.S. DOLLARS

SINCE FILE

TOTAL

ENTRY

SESSION

FULL ESTIMATED COST

0.21

0.21

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DICTIONARY FILE UPDATES: 22 SEP 2002 HIGHEST RN 453594-96-2

TSCA INFORMATION NOW CURRENT THROUGH MAY 20, 2002

Please note that search-term pricing does apply when conducting SmartSELECT searches.

Crossover limits have been increased. See HELP CROSSOVER for details.

Experimental and calculated property data are now available. See HELP PROPERTIES for more information. See STN Note 27, Searching Properties in the CAS Registry File, for complete details:

<http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf>

=>

Uploading 534893 (formula iv broad).str

L1 STRUCTURE UPLOADED

=> d

L1 HAS NO ANSWERS

L1 STR

\* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT \*

Structure attributes must be viewed using STN Express query preparation.

=> s l1

SAMPLE SEARCH INITIATED 08:08:11 FILE 'REGISTRY'

SAMPLE SCREEN SEARCH COMPLETED - 4 TO ITERATE

100.0% PROCESSED 4 ITERATIONS

1 ANSWERS

SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE \*\*COMPLETE\*\*

BATCH \*\*COMPLETE\*\*

PROJECTED ITERATIONS: 4 TO 200

PROJECTED ANSWERS: 1 TO 80

L2 1 SEA SSS SAM L1

=> s l1 full

FULL SEARCH INITIATED 08:08:17 FILE 'REGISTRY'

FULL SCREEN SEARCH COMPLETED - 133 TO ITERATE

100.0% PROCESSED 133 ITERATIONS  
SEARCH TIME: 00.00.01

63 ANSWERS

L3 63 SEA SSS FUL L1

=&gt; fil stnguide

COST IN U.S. DOLLARS

SINCE FILE

TOTAL

ENTRY

SESSION

FULL ESTIMATED COST

141.04

141.25

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FILE CONTAINS CURRENT INFORMATION.

LAST RELOADED: Sep 20, 2002 (20020920/UP).

=&gt; fil reg

COST IN U.S. DOLLARS

SINCE FILE

TOTAL

ENTRY

SESSION

FULL ESTIMATED COST

0.18

141.43

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DICTIONARY FILE UPDATES: 22 SEP 2002 HIGHEST RN 453594-96-2

TSCA INFORMATION NOW CURRENT THROUGH MAY 20, 2002

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conducting SmartSELECT searches.

Crossover limits have been increased. See HELP CROSSOVER for details.

Experimental and calculated property data are now available. See HELP  
PROPERTIES for more information. See STNote 27, Searching Properties  
in the CAS Registry File, for complete details:  
<http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf>

=&gt;

Uploading 534893 (formula iv broad).str

L4 STRUCTURE UPLOADED

=&gt; d

L4 HAS NO ANSWERS

L4 STR

\* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT \*

Structure attributes must be viewed using STN Express query preparation.

=&gt; s l4

SAMPLE SEARCH INITIATED 08:11:16 FILE 'REGISTRY'  
SAMPLE SCREEN SEARCH COMPLETED - 9 TO ITERATE

100.0% PROCESSED 9 ITERATIONS  
SEARCH TIME: 00.00.01

1 ANSWERS

FULL FILE PROJECTIONS: ONLINE \*\*COMPLETE\*\*  
BATCH \*\*COMPLETE\*\*  
PROJECTED ITERATIONS: 9 TO 360  
PROJECTED ANSWERS: 1 TO 80

L5 1 SEA SSS SAM L4

=> s 15 full  
FULL SEARCH INITIATED 08:11:37 FILE 'REGISTRY'  
FULL SCREEN SEARCH COMPLETED - 193 TO ITERATE

100.0% PROCESSED 193 ITERATIONS  
SEARCH TIME: 00.00.01

45 ANSWERS

L6 45 SEA SSS FUL L4

=> d scan

L6 45 ANSWERS REGISTRY COPYRIGHT 2002 ACS  
 IN Cyclo[N2-methyl-L-arginylglycyl-L-.alpha.-aspartyl-3-(aminomethyl)-5-[[1-oxo-6-[[[6-[[[2-sulphophenyl)methylene]hydrazino]-3-pyridinyl]carbonyl]amino]hexyl]amino]benzoyl-D-valyl], monoacetate, monoammonium salt (9CI)

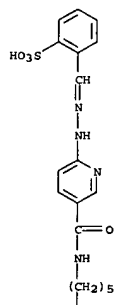
SOL 5  
 MF C45 H59 N13 O12 S . C2 H4 O2 . H3 N

\*\*RELATED SEQUENCES AVAILABLE WITH SEQLINK\*\*

CM 1

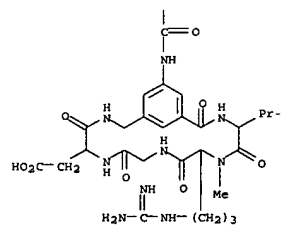
\*\*RELATED SEQUENCES AVAILABLE WITH SEQLINK\*\*

PAGE 1-A



L6 45 ANSWERS REGISTRY COPYRIGHT 2002 ACS (Continued)

PAGE 2-A



CM 2



HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):end

09/534,893

<page

=> d l c 1-

YOU HAVE REQUESTED DATA FROM 45 ANSWERS - CONTINUE? Y/(N):y



L6 ANSWER 1 OF 45 REGISTRY COPYRIGHT 2002 ACS  
LC STN Files: CA, CAPLUS

L6 ANSWER 2 OF 45 REGISTRY COPYRIGHT 2002 ACS  
LC STN Files: CA, CAPLUS

L6 ANSWER 3 OF 45 REGISTRY COPYRIGHT 2002 ACS  
LC STN Files: CA, CAPLUS

L6 ANSWER 4 OF 45 REGISTRY COPYRIGHT 2002 ACS  
LC STN Files: CA, CAPLUS

09/534,893

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LC STN Files: CA, CAPLUS

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LC STN Files: CA, CAPLUS

L6 ANSWER 8 OF 45 REGISTRY COPYRIGHT 2002 ACS  
LC STN Files: CA, CAPLUS, USPATFULL

09/534,893

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L6 ANSWER 11 OF 45 REGISTRY COPYRIGHT 2002 ACS  
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L6 ANSWER 12 OF 45 REGISTRY COPYRIGHT 2002 ACS  
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L6 ANSWER 20 OF 45 REGISTRY COPYRIGHT 2002 ACS

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L6 ANSWER 22 OF 45 REGISTRY COPYRIGHT 2002 ACS

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LC STN Files: CA, CAPLUS, USPATFULL

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L6 ANSWER 36 OF 45 REGISTRY COPYRIGHT 2002 ACS  
LC STN Files: CA, CAPLUS, USPATFULL

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LC STN Files: CA, CAPLUS, USPATFULL

L6 ANSWER 39 OF 45 REGISTRY COPYRIGHT 2002 ACS  
LC STN Files: CA, CAPLUS, CASREACT, USPATFULL

L6 ANSWER 40 OF 45 REGISTRY COPYRIGHT 2002 ACS  
LC STN Files: CA, CAPLUS

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L6 ANSWER 41 OF 45 REGISTRY COPYRIGHT 2002 ACS  
LC STN Files: CA, CAPLUS, USPATFULL

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LC STN Files: CA, CAPLUS, USPATFULL

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LC STN Files: CA, CAPLUS, USPATFULL

L6 ANSWER 44 OF 45 REGISTRY COPYRIGHT 2002 ACS

09/534,893

<page

L6 ANSWER 45 OF 45 REGISTRY COPYRIGHT 2002 ACS  
LC STN Files: CA, CAPLUS, USPATFULL

=> fil .search  
COST IN U.S. DOLLARS

SINCE FILE	TOTAL
ENTRY	SESSION
212.52	353.95

FULL ESTIMATED COST

FILE 'MEDLINE' ENTERED AT 08:12:58 ON 24 SEP 2002

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=> d his

(FILE 'HOME' ENTERED AT 08:07:06 ON 24 SEP 2002)

FILE 'REGISTRY' ENTERED AT 08:07:11 ON 24 SEP 2002

L1 STRUCTURE UPLOADED  
L2 1 S L1  
L3 63 S L1 FULL

FILE 'STNGUIDE' ENTERED AT 08:08:48 ON 24 SEP 2002

FILE 'REGISTRY' ENTERED AT 08:10:47 ON 24 SEP 2002

L4 STRUCTURE UPLOADED  
L5 1 S L4  
L6 45 S L5 FULL

FILE 'MEDLINE, CAPLUS, BIOSIS, USPATFULL, EMBASE' ENTERED AT 08:12:58 ON  
24 SEP 2002

=> s l6

L7 23 L6

=> dup rem l7

PROCESSING COMPLETED FOR L7

L8 20 DUP REM L7 (3 DUPLICATES REMOVED)

=> d ibib ab hitstr 1-

YOU HAVE REQUESTED DATA FROM 20 ANSWERS - CONTINUE? Y/(N):y

L8 ANSWER 1 OF 20 USPATFULL  
ACCESSION NUMBER: 2002:21796 USPATFULL  
TITLE: Ternary ligand complexes useful as  
radiopharmaceuticals  
INVENTOR(S): Liu, Shuang, Chelmsford, MA, UNITED STATES

PAGE 1-A

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2002012631	A1	20020131
APPLICATION INFO.:	US 2001-826449	A1	20010405 (9)

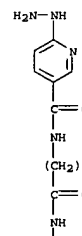
	NUMBER	DATE
PRIORITY INFORMATION:	US 2000-195235P	20000407 (60)
DOCUMENT TYPE:	Utility	
FILE SEGMENT:	APPLICATION	
LEGAL REPRESENTATIVE:	Dupont Pharmaceuticals Company, Legal Department - Patents, 1007 Market Street, Wilmington, DE, 19898	
NUMBER OF CLAIMS:	47	
EXEMPLARY CLAIM:	1	
LINE COUNT:	2595	

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

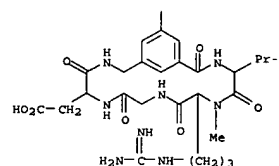
AB This invention relates to novel highly functionalized phosphine ligands as ancillary ligands in radiopharmaceuticals. Also, this invention provides radiopharmaceuticals comprised of highly functionalized phosphine ligated sup.99mTc labeled HYNIC-conjugated biomolecules that selectively localize at sites of disease and thus allow an image to be obtained of the loci using gamma scintigraphy. The invention also provides methods of use of the radiopharmaceuticals as imaging agents for the diagnosis of cardiovascular disorders such as thromboembolic disease or atherosclerosis, infectious disease and cancer.

IT 167214-98-4P  
(for prepn. of technetium-99m radiopharmaceuticals contg. highly functionalized phosphines, HYNIC-conjugated biomols., and tricine ligands as diagnostic imaging agents)

RN 167214-98-4 USPATFULL  
CN Cyclo[3-(aminomethyl)-5-[[[6-[[[6-hydrazino-3-pyridinyl]carbonyl]amino]-1-oxohexyl]amino]benzoyl]-D-valyl-N2-methyl-L-arginylglycyl-L-.alpha.-aspartyl] (9CI) (CA INDEX NAME)



PAGE 2-A



L8 ANSWER 2 OF 20 CAPLUS COPYRIGHT 2002 ACS  
ACCESSION NUMBER: 2001:763010 CAPLUS  
DOCUMENT NUMBER: 135:312738  
TITLE: Ternary ligand complexes containing highly functionalized triphenylphosphines useful as radiopharmaceuticals  
INVENTOR(S): Liu, Shuang  
PATENT ASSIGNEE(S): Dupont Pharmaceuticals Company, USA  
SOURCE: PCT Int. Appl., 210 pp.  
CODON: P1XXD2  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001077122	A1	20011018	WO 2001-US11387	20010406
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CP, CO, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 2002012631	A1	20020131	US 2001-826449	20010405

PRIORITY APPLN. INFO.: US 2000-195235P P 20000407  
OTHER SOURCE(S): MARPAT 135:312738

AB This invention relates to novel highly functionalized triphenylphosphine ligands as ancillary ligands in radiopharmaceuticals. Also, this invention provides radiopharmaceuticals comprised of highly functionalized

phosphine ligated 99mTc labeled hydrazinonicotinamide (HYNIC)-conjugated biomols. that selectively localize at sites of disease and thus allow an image to be obtained of the loci using gamma scintigraphy. The chelator-modified biomols. include 11b/11fa antagonists, tuftsin, receptor

antagonists, chemotactic peptides, vitronectin receptor antagonists, tyrosine kinase inhibitors, and aminocarboxylates. The invention also provides methods of use of the radiopharmaceuticals as imaging agents for the diagnosis of cardiovascular disorders such as thromboembolic disease or atherosclerosis, infectious disease and cancer. The invention further provides kits for the prepn. of the radiopharmaceuticals. The highly functionalized phosphines contain hydroxy or polyhydroxy functionalities which are of interest because they can form neutral 99mTc complexes. The highly functionalized phosphines can contain carboxy or polycarboxy functionalities which are used to increase hydrophilicity and to improve blood clearance and renal excretion of the 99mTc-labeled biomol. The highly functionalized phosphines can also contain metabolizable ester or polyester functionalities and form neutral 99mTc complexes (if there is no

charge on the biomol.), which can cross the cell membrane and potentially bind intracellular receptors. In an example, the functionalized ligand P(C6H4(CONHCH2CH2OH)-p)3 (L3) was prepd. The ligand was reacted with [99mTc]pertechnetate in the presence of HYNIC-Ln-O, a HYNIC-conjugated biomol., and with tricine, to give [99mTc(HYNIC-Ln-O)(tricine)(L3)] in >70% yield.

IT 167214-98-4P

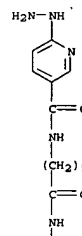
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT

L8 ANSWER 1 OF 20 USPATFULL (Continued)

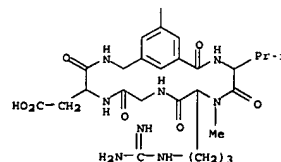
L8 ANSWER 2 OF 20 CAPLUS COPYRIGHT 2002 ACS (Continued)  
(Reactant or reagent)  
(for prepn. of technetium-99m radiopharmaceuticals contg. highly functionalized phosphines, HYNIC-conjugated biomols., and tricine ligands as diagnostic imaging agents)

RN 167214-98-4 CAPLUS  
CN Cyclo[3-(aminomethyl)-5-[[[6-[[[6-hydrazino-3-pyridinyl]carbonyl]amino]-1-oxohexyl]amino]benzoyl]-D-valyl-N2-methyl-L-arginylglycyl-L-.alpha.-aspartyl] (9CI) (CA INDEX NAME)

PAGE 1-A



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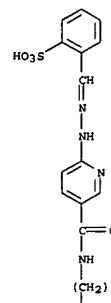


REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE  
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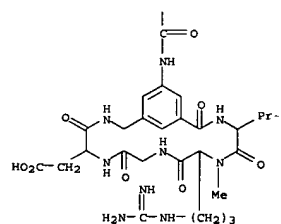
L8 ANSWER 3 OF 20 CAPLUS COPYRIGHT 2002 ACS  
 ACCESSION NUMBER: 2001:128752 CAPLUS  
 DOCUMENT NUMBER: 135:9967  
 TITLE: Towards developing a non-SnCl<sub>2</sub> formulation for RP444, a new radiopharmaceutical for thrombus imaging  
 AUTHOR(S): Liu, Shuang; Edwards, Scott; Harris, Anthony R.; Ziegler, Marissa C.; Poirier, Michael J.; Ewels, Barbara A.; Diluzio, Willow R.; Hui, Poh  
 CORPORATE SOURCE: Medical Imaging Division, DuPont Pharmaceuticals Company, North Billerica, MA, 01862, USA  
 SOURCE: Journal of Pharmaceutical Sciences (2001), 90(2), 114-123  
 CODEN: JPMSAE; ISSN: 0022-3549  
 PUBLISHER: Wiley-Liss, Inc.  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 AB There are many factors influencing the yield and radiochem. purity (RCP) of the radiopharmaceutical RP444. These include heating temp., heating time, pH, the use of a buffering agent and a bulking agent, as well as the component (XV066, tricine, TPPTS, and Na<sup>99m</sup>TcO<sub>4</sub>) concn. Through a series of radiolabeling expts., we found that a formulation comprised of 20 .mu.g of XV066, 6.5 mg of tricine, 40 mg of mannitol, 5 mg of TPPTS, and 0.1 mg of Pluronic acid dissolved in 1.0 mL of 250 mM succinate buffer (pH 5.0) gives the best RCP for RP444. The formulation can be lyophilized to form a stable crystal "cake". The radiolabeling is achieved by adding 1.5 mL generator eluant (33-133 mCi of Na<sup>99m</sup>TcO<sub>4</sub>) to a lyophilized vial and heating the reaction mixt. at 100.degree.C for 10 min. Using this formulation, RP444 is prepd. consistently in high yield with RCP .gtoreq. 90%. Formation of (99mTc)colloid is minimal (<0.5%).  
 IT 186305-30-6  
 RL: RCT (Reactant); RACT (Reactant or reagent) (developing a non-SnCl<sub>2</sub> formulation for RP444 radiopharmaceutical for thrombus imaging)  
 RN 186305-30-6 CAPLUS  
 CN Cyclo[N2-methyl-L-arginylglycyl-L-.alpha.-aspartyl-3-(aminomethyl)-5-[[1-oxo-6-[[[6-[[[2-sulfophenyl)methylene]hydrazino]-3-pyridinyl]carbonyl]amino]hexyl]amino]benzoyl-D-valyl], monosodium salt (9CI) (CA INDEX NAME)

L8 ANSWER 3 OF 20 CAPLUS COPYRIGHT 2002 ACS (Continued)

PAGE 1-A



PAGE 2-A



● Na

REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE REFORMAT

L8 ANSWER 3 OF 20 CAPLUS COPYRIGHT 2002 ACS (Continued)

L8 ANSWER 4 OF 20 CAPLUS COPYRIGHT 2002 ACS  
 ACCESSION NUMBER: 2000:260317 CAPLUS  
 DOCUMENT NUMBER: 132:294012  
 TITLE: Process for cyclic peptide for use as thrombus agent  
 INVENTOR(S): Bishop, John  
 PATENT ASSIGNEE(S): Du Pont Pharmaceuticals Company, USA  
 SOURCE: PCT Int. Appl., 68 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000021982	A1	20000420	WO 1999-US21628	19991013
W:	AL, AU, BR, CA, CN, CZ, EE, HU, IL, IN, JP, KR, LT, LV, MX, NO, NZ, PL, RO, SG, SI, SK, TR, UA, VN, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RM:	AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE			
AU 9963938	A1	20000501	AU 1999-63938	19991013
EP 1121378	A1	20010808	EP 1999-951511	19991013
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO			
JP 2002527451	T2	20020827	JP 2000-575887	19991013
PRIORITY APPLN. INFO.:			US 1998-103921P	19981013
			WO 1999-US21628	19991013

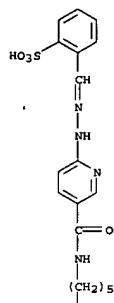
OTHER SOURCE(S): CASREACT 132:294012  
 AB A process is described for the synthesis of cyclic peptide I, which serves as an imaging agent for the diagnosis of cardiovascular disorders, infection, inflammation, and cancer. The key step involves cyclization of intermediate II (Ts = tosyl, Boc = tert-butoxycarbonyl).  
 IT 264217-41-6P  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent) (process for cyclic peptide for use as thrombus imaging agent)  
 RN 264217-41-6 CAPLUS  
 CN Cyclo[N2-methyl-L-arginylglycyl-L-.alpha.-aspartyl-3-(aminomethyl)-5-[[1-oxo-6-[[[6-[[[2-sulfophenyl)methylene]hydrazino]-3-pyridinyl]carbonyl]amino]hexyl]amino]benzoyl-D-valyl], monoacetate, monoammonium salt (9CI) (CA INDEX NAME)

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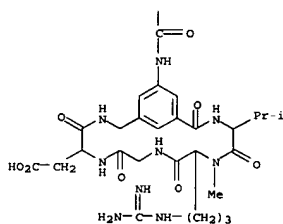
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L8 ANSWER 4 OF 20 CAPLUS COPYRIGHT 2002 ACS (Continued)

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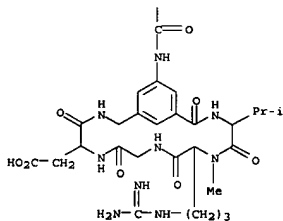


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CMP C2 H4 O2

L8 ANSWER 4 OF 20 CAPLUS COPYRIGHT 2002 ACS (Continued)

PAGE 2-A



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L8 ANSWER 4 OF 20 CAPLUS COPYRIGHT 2002 ACS (Continued)



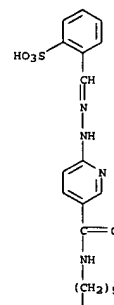
IT 186304-77-8P

RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
(process for cyclic peptide for use as thrombus imaging agent)

RN 186304-77-8 CAPLUS

CN Cyclo[N2-methyl-L-arginylglycyl-L-.alpha.-aspartyl-3-(aminomethyl)-5-[[1-oxo-6-[[[6-[[[2-sulfophenyl)methylene]hydrazino]-3-pyridinyl]carbonyl]amino]hexyl]amino]benzoyl-D-valyl] (9CI) (CA INDEX NAME)

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L8 ANSWER 5 OF 20 USPATFULL

ACCESSION NUMBER: 2000:15299 USPATFULL

TITLE: Radiolabeled platelet GPIIb/IIIa receptor antagonists as imaging agents for the diagnosis of thromboembolic disorders

INVENTOR(S): DeGrado, William Frank, Moylan, PA, United States  
Mousa, Shaker Ahmed, Lincoln University, PA, United States  
Sworin, Michael, Newark, DE, United States  
Barrett, John Andrew, West Groton, MA, United States  
Edwards, Scott David, Burlington, MA, United States  
Harris, Thomas David, Salem, NH, United States  
Rajopadhye, Milind, Westford, MA, United States  
Liu, Shuang, Chelmsford, MA, United States  
DuPont Pharmaceuticals Company, Wilmington, DE, United States (U.S. corporation)

PATENT ASSIGNEE(S): DuPont Pharmaceuticals Company, Wilmington, DE, United States (U.S. corporation)

NUMBER	KIND	DATE
US 6022523		20000208
US 1997-999400		19971229 (8)
Continuation of Ser. No. US 1994-218861, filed on 28 Mar 1994, now patented, Pat. No. US 5879657 which is a continuation-in-part of Ser. No. US 1993-40336, filed on 30 Mar 1993, now abandoned		
DOCUMENT TYPE: Utility		
FILE SEGMENT: Granted		
PRIMARY EXAMINER: Tsang, Cecilia J.		
ASSISTANT EXAMINER: Jameison, Fabian A.		
LEGAL REPRESENTATIVE: Boudreaux, G. Jess, Vance, David H.		
NUMBER OF CLAIMS: 1		
EXEMPLARY CLAIM: 1		
NUMBER OF DRAWINGS: 2 Drawing Figure(s); 1 Drawing Page(s)		
LINE COUNT: 6906		
CAS INDEXING IS AVAILABLE FOR THIS PATENT.		
AB This invention provides novel radiopharmaceuticals that are radiolabeled		
cyclic compounds containing carbocyclic or heterocyclic ring systems which act as antagonists of the platelet glycoprotein IIb/IIIa complex; to methods of using said radiopharmaceuticals as imaging agents for the diagnosis of arterial and venous thrombi; to novel reagents for the preparation of said radiopharmaceuticals; and to kits comprising said reagents.		

IT 167214-98-40P, technetium-99m complex  
(prepn. of radiolabeled platelet GPIIb/IIIa receptor antagonists as imaging agents for the diagnosis of thromboembolic disorders)

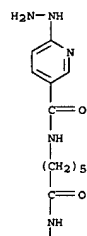
RN 167214-98-4 USPATFULL

CN Cyclo[3-(aminomethyl)-5-[[[6-[[[6-hydrazino-3-pyridinyl]carbonyl]amino]-1-oxohexyl]amino]benzoyl-D-valyl-N2-methyl-L-arginylglycyl-L-.alpha.-aspartyl] (9CI) (CA INDEX NAME)

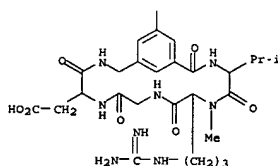


L8 ANSWER 5 OF 20 USPATFULL (Continued)

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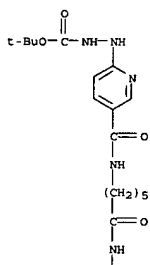
PAGE 2-A



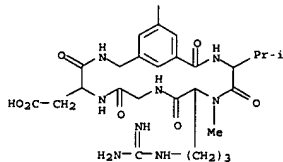
IT 167214-98-4P 167215-94-3P 167356-24-3P  
 (prepn. of radiolabeled platelet GPIIb/IIIa receptor antagonists as  
 imaging agents for the diagnosis of thromboembolic disorders)  
 RN 167214-98-4 USPATFULL  
 CN Cyclo[3-(aminomethyl)-5-[[6-[[[(6-hydrazino-3-pyridinyl)carbonyl]amino]-1-oxohexyl]amino]benzoyl-D-valyl-N2-methyl-L-arginylglycyl-L-.alpha.-aspartyl] (9CI) (CA INDEX NAME)

L8 ANSWER 5 OF 20 USPATFULL (Continued)

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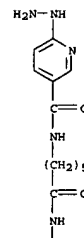


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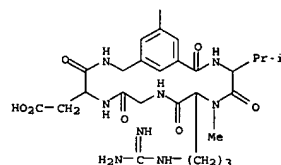


L8 ANSWER 5 OF 20 USPATFULL (Continued)

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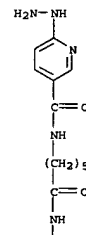
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 CMP C43 H63 N13 O11

L8 ANSWER 5 OF 20 USPATFULL (Continued)

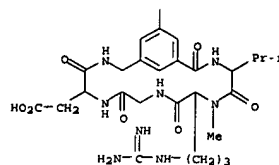
RN 167356-24-3 USPATFULL  
 CN L-Aspartic acid, N-[3-(aminomethyl)-5-[[6-[[[(6-hydrazino-3-pyridinyl)carbonyl]amino]-1-oxohexyl]amino]benzoyl-D-valyl-N2-methyl-L-arginylglycyl-, cyclic (41.fwdarw.1)-peptide, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1  
 CRN 167214-98-4  
 CMP C38 H55 N13 O9  
 CDES \*

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CM 2

L8 ANSWER 5 OF 20 USPATFULL (Continued)

CRN 76-05-1  
CMP C2 H P3 O2

L8 ANSWER 6 OF 20 USPATFULL

ACCESSION NUMBER: 2000:7405 USPATFULL  
TITLE: Stable reagents for the preparation of radio pharmaceuticals  
INVENTOR(S): Sworin, Michael, 22 Appaloosa Cir., Tyngeboro, MA, United States 01879  
Rajopadhye, Milind, 21 Honeysuckle Rd., Westford, MA, United States 01886  
Harris, Thomas David, 56 Zion Hill Rd., Salem, NH, United States 03079  
Edwards, David Scott, 123 Farms Dr., Burlington, MA, United States 01803  
Cheesman, Edward Hollister, 55 Turkey Hill Rd., Lunenburg, MA, United States 01462  
Liu, Shuang, 17 Judith Rd., Chelmsford, MA, United States 01864

NUMBER	KIND	DATE
US 6015904		20000118
US 1997-956313		19971023 (8)
PATENT INFORMATION: Division of Ser. No. US 1995-476296, filed on 7 Jun 1995, now patented, Pat. No. US 5750088 which is a continuation-in-part of Ser. No. US 1994-218861, filed on 28 Mar 1994, now patented, Pat. No. US 5879657		

which

is a continuation-in-part of Ser. No. US 1993-40336, filed on 30 Mar 1993, now abandoned

DOCUMENT TYPE: Utility  
FILE SEGMENT: Granted  
PRIMARY EXAMINER: Dees, Josee' G.  
ASSISTANT EXAMINER: Hartley, Michael G.  
NUMBER OF CLAIMS: 11  
EXEMPLARY CLAIM: 1  
NUMBER OF DRAWINGS: 1 Drawing Figure(s); 1 Drawing Page(s)  
LINE COUNT: 1847

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB This invention provides novel reagents for the preparation of radiopharmaceuticals useful as imaging agents for the diagnosis of cardiovascular disorders, infection, inflammation and cancer, diagnostic

kits comprising said reagents and intermediate compounds useful for the preparation of said reagents. The reagents are comprised of stable hydrazone modified biologically active molecules that react with gamma emitting radioisotopes to form radiopharmaceuticals that selectively localize at sites of disease and thus allow an image to be obtained of the loci using gamma scintigraphy.

IT 167214-98-4DP, technetium-99m complex  
(prepn. of radiolabeled platelet GPIIb/IIIa receptor antagonists as imaging agents for the diagnosis of thromboembolic disorders)

RN 167214-98-4 USPATFULL

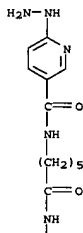
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L8 ANSWER 6 OF 20 USPATFULL (Continued)

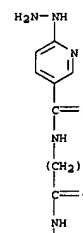
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L8 ANSWER 6 OF 20 USPATFULL (Continued)

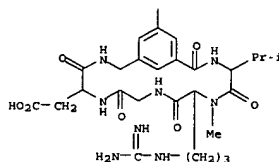
PAGE 1-A



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IT 167214-98-4P 167215-94-3P 167356-24-3P  
(prepn. of radiolabeled platelet GPIIb/IIIa receptor antagonists as imaging agents for the diagnosis of thromboembolic disorders)

RN 167214-98-4 USPATFULL

CN Cyclo[3-(aminomethyl)-5-[[6-[[[(6-hydrazino-3-pyridinyl)carbonyl]amino]-1-oxohexyl]amino]benzoyl-D-valyl-N2-methyl-L-arginylglycyl-L-.alpha.-aspartyl]] (9CI) (CA INDEX NAME)

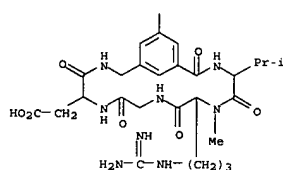
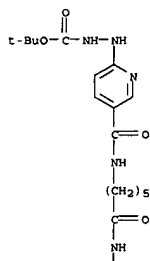
RN 167215-94-3 USPATFULL

CN L-Aspartic acid, N-[3-(aminomethyl)-5-[[6-[[[(6-hydrazino-3-pyridinyl)carbonyl]amino]-1-oxohexyl]amino]benzoyl]-D-valyl-N2-methyl-L-arginylglycyl-, cyclic (41.fwdarw.1)-peptide, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

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CRN 167215-93-2  
CMP C43 H63 N13 O11

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CRN 76-05-1

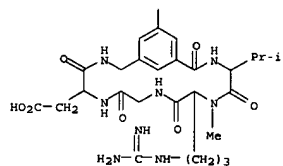
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PAGE 1-A

LS ANSWER 6 OF 20 USPATFULL (Continued)

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CM 2

CRN 76-05-1

CMF C2 H F3 O2



LB ANSWER 6 OF 20 USPATFULL (Continued)



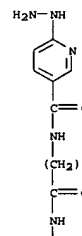
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arginylglycyl-, cyclic (41.fdwdr.w.1)-peptide, mono(trifluoroacetate)
(SC1)  (CA INDEX NAME)

CM      1

CWN     167214-98-4
CMP      C38 H55 N13 O9
CDES     *

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180: ANSWER 7 OF 20 USPATFULL

3000:1522 USPATFULL

ACCESSION NUMBER: Ternary radiopharmaceutical complexes

TITLE: Edwards, David Scott, 123 Farms Dr., Burlington, MA, United States 01803

INVENTOR(S): Liu, Shuang, 17 Judith Rd., Chelmsford, MA, United States 01824

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 6010679		200008104
APPLICATION INFO.:	US 1998-13320		19980126 (9)
RELATED APPLN. INFO.:	Continuation of Ser. No. US 1995-415908, filed on 3 Apr 1995, now patented, Pat. No. US 5744120 which is a continuation-in-part of Ser. No. US 1994-218861, filed on 28 Mar 1994, now patented, Pat. No. US 5879657		

which is a continuation-in-part of Ser. No. US 1993-40336, filed on 30 Mar 1993, now abandoned

DOCUMENT TYPE: Utility

FILE SEGMENT: Granted

PRIMARY EXAMINER: Dees, Jose' G.

ASSISTANT EXAMINER: Jones, Dameron

NUMBER OF CLAIMS: 15

EXEMPLARY CLAIM: 1

LINE COUNT: 1664

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB This invention provides novel radiopharmaceuticals which are useful as imaging agents for the diagnosis of cardiovascular disorders, infectious disease and cancer. The radiopharmaceuticals are comprised of phosphine or arsine ligated technetium-99m labeled hydrazino or diazino modified biologically active molecules that selectively localize at sites of disease and thus allow an image to be obtained of the loci using gamma scintigraphy. This invention also provides methods for using the radiopharmaceuticals and kits comprising radiopharmaceutical precursors.

The radiopharmaceuticals of this invention have the structure:

$$[(Q).sub.d \cdot (L).sub.n - C.sub.h \cdot ].sub.x \cdot -M.sub.t \cdot (A.sub.L1).sub.y \cdot (A.sub.L2).z;$$

wherein the variables are as defined herein.

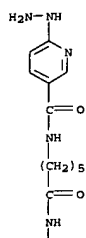
IT 167214-98-4DP, technetium-99m complex  
(prepn. of radiolabeled platelet GPIIb/IIIa receptor antagonists as imaging agents for the diagnosis of thromboembolic disorders)

RN 167214-98-4 USPATFULL

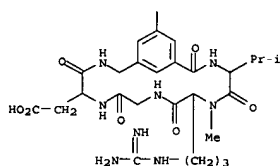
CN Cyclo[3-(aminomethyl)-5-[[6-[(6-hydrazino-3-pyridinyl)carbonyl]amino]-1-oxohexyl]amino]benzoyl-D-valyl-N2-methyl-L-arginylglycyl-L-.alpha.-aspartyl] (9CI) [CA INDEX NAME]

L8 ANSWER 7 OF 20 USPATFULL (Continued)

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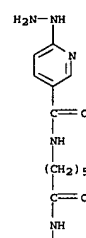
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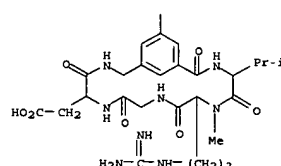
IT 167214-98-4P 167215-94-3P 167356-24-3P  
 [prepn. of radiolabeled platelet GPIIb/IIIa receptor antagonists as  
 imaging agents for the diagnosis of thromboembolic disorders]  
 RN 167214-98-4 USPATFULL  
 CN Cyclo[3-(aminomethyl)-5-[[6-[[[(6-hydrazino-3-pyridinyl)carbonyl]amino]-1-oxohexyl]amino]benzoyl]-D-valyl-N2-methyl-L-arginylglycyl-L-.alpha.-aspartyl] (9CI) (CA INDEX NAME)

L8 ANSWER 7 OF 20 USPATFULL (Continued)

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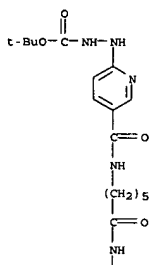
PAGE 2-A



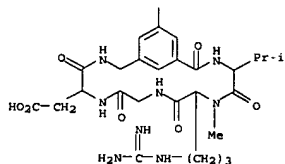
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 CM 1  
 CRN 167215-93-2  
 CMF C43 H63 N13 O11

L8 ANSWER 7 OF 20 USPATFULL (Continued)

PAGE 1-A



PAGE 2-A



CM 2  
 CRN 76-05-1  
 CMF C2 H F3 O2

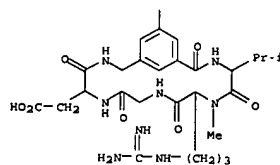
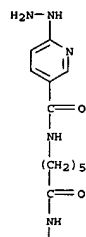


L8 ANSWER 7 OF 20 USPATFULL (Continued)

PAGE 1-A

RN 167356-24-3 USPATFULL  
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 CM 1  
 CRN 167214-98-4  
 CMF C38 H55 N13 O9  
 CDES \*

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CM 2

L8 ANSWER 7 OF 20 USPATFULL (Continued)

CRN 76-05-1  
CMP C3 H P3 O2

L8 ANSWER 8 OF 20 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 1

ACCESSION NUMBER: 1999:181611 CAPLUS  
DOCUMENT NUMBER: 130:237883  
TITLE: Preparation of radiolabeled platelet GPIIb/IIIa receptor antagonists as imaging agents for the diagnosis of thromboembolic disorders  
INVENTOR(S): Degrado, William Frank; Mousa, Shaker Ahmed; Sworin, Michael; Barrett, John Andrew; Edwards, Scott David; Harris, Thomas David; Rajopadhye, Milind; Liu, Shuang  
PATENT ASSIGNEE(S): The Dupont Merck Pharmaceutical Company, USA  
SOURCE: U.S., 135 pp., Cont.-in-part of U.S. Ser. No. 40,336, abandoned.  
CODEN: USXXAM  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 6  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5879657	A	19990309	US 1994-218861	19940328
CA 2159445	AA	19941013	CA 1994-2159445	19940329
WO 9422494	A1	19941013	WO 1994-US3256	19940329
W: AU, BB, BG, BR, BY, CA, CN, CZ, FI, GE, HU, JP, KG, KP, KR, KZ, LK, LV, MD, MG, MN, MW, NO, NZ, PL, RO, RU, SD, SI, SK, TJ, TT, UA, UZ, VN				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9465248	A1	19941024	AU 1994-65248	19940329
EP 692982	A1	19960124	EP 1994-912870	19940329
EP 692982	B1	20000705		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
CN 1122577	A	19960515	CN 1994-192010	19940329
HU 72889	A2	19960628	HU 1995-2862	19940329
BR 9406055	A	19960910	BR 1994-6055	19940329
BR 9406820	A	19960910	BR 1994-6820	19940329
JP 08509710	T2	19961015	JP 1994-522205	19940329
JP 3042887	B2	20000522		
RO 114895	B1	19990830	RO 1995-1701	19940329
RU 2145608	C1	20000220	RU 1995-118183	19940329
EP 995761	A2	20000426	EP 1999-116915	19940329
EP 995761	A3	20000712		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, SE, MC, PT, IE, SI				
AT 194293	E	20000715	AT 1994-912870	19940329
ES 2149265	T3	20001101	ES 1994-912870	19940329
ZA 9402262	A	19951002	ZA 1994-2262	19940330
TW 445267	B	20010711	TW 1994-83104199	19940507
US 5744120	A	19980428	US 1995-415908	19950403
US 5750088	A	19980512	US 1995-476296	19950607
FI 9504655	A	19951102	FI 1995-4655	19950929
NO 9503886	A	19951130	NO 1995-3886	19950929
LV 11106	B	19970420	LV 1995-296	19951027
AU 9534525	A1	19960321	AU 1995-34525	19951030
AU 689643	B2	19980402		
US 6015904	A	20000118	US 1997-956313	19971023

L8 ANSWER 8 OF 20 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 1  
(Continued)

US 6022523 A 20000208 US 1997-999400 19971229  
US 6010679 A 20000104 US 1998-13320 19980126  
PRIORITY APPLN. INFO.:  
US 1993-40336 B2 19930330  
US 1994-218861 A 19940328  
EP 1994-912870 A3 19940329  
WO 1994-US3256 W 19940329  
US 1995-415908 A1 19950403  
US 1995-476296 A3 19950607

OTHER SOURCE(S): MARPAT 130:237883  
AB Reagents for prepg. radiopharmaceuticals (Q-LG)d-X, Qe-LG-X [d = 1-3; e = 2-20; LG = linking group; X = metal chelator; Q = Q1; R11 = (substituted) satd., partially satd., or arom. carbocyclyl, heterocyclyl, optionally bonded to LG; R12 = CO, CS, SO2, P(=2)(ZR13); Z = S, O; m, n = 0-2; R1, R22 = H, (substituted) alkyl, alkenyl, alkynyl, cycloalkyl, aryl, heterocyclyl, iO, F, Cl, Br, iodo, CF3, cyano, bond to LG, etc.; R1R21, R2R23 = atoms to form a (substituted) 3-7 membered carbocyclyl; R1R2 = atoms to form a (substituted) 5-8 membered ring; R21, R23 = H, (halo)alkyl, PhCH2; R13 = H, alkyl, cycloalkyl, alkylcycloalkyl, aryl, alkylaryl, alkoxyalkyl; R2 = H, alkyl; J = .beta.-Ala, defined .alpha.-amino acid residue; K, M = defined .alpha.-amino acid residue; L =

Y(CH2)vCO; Y = imino, O, S; v = 1, 2], and the pharmaceuticals themselves.  
were prepd. Thus, technetium complex I (prepn. given) was used at 1 mCi/Kg i.v. for imaging jugular thrombi in dogs.

IT 167214-98-4DP, technetium-99m and EDDA complex

167214-98-4P 221276-20-6P

RL: BAC (Biological activity or effector, except adverse); BSU

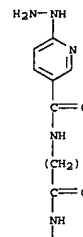
(Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses) (prepn. of radiolabeled platelet GPIIb/IIIa receptor antagonists as imaging agents for the diagnosis of thromboembolic disorders)

RN 167214-98-4 CAPLUS

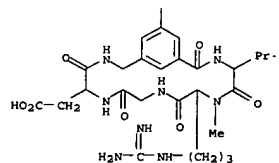
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L8 ANSWER 8 OF 20 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 1  
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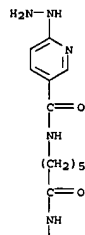


RN 167214-98-4 CAPLUS  
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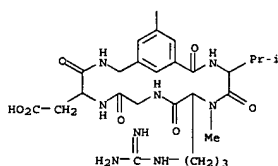
L8 ANSWER 8 OF 20 CAPLUS COPYRIGHT 2002 ACS  
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DUPLICATE 1

PAGE 1-A



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RN 221276-20-6 CAPLUS  
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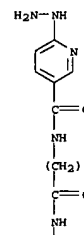
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CRN 167214-98-4  
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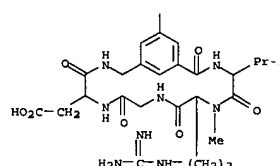
L8 ANSWER 8 OF 20 CAPLUS COPYRIGHT 2002 ACS  
(Continued)

DUPLICATE 1

PAGE 1-A



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CM 2

CRN 76-05-1  
CMP C2 H F3 O2

L8 ANSWER 8 OF 20 CAPLUS COPYRIGHT 2002 ACS  
(Continued)

DUPLICATE 1



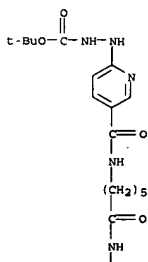
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RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
(prepn. of radiolabeled platelet GPIIb/IIIa receptor antagonists as imaging agents for the diagnosis of thromboembolic disorders)

RN 221276-23-9 CAPLUS  
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CRN 167215-93-2  
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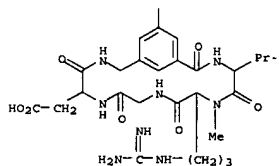
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L8 ANSWER 8 OF 20 CAPLUS COPYRIGHT 2002 ACS  
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DUPLICATE 1

PAGE 2-A



CM 2

CRN 76-05-1  
CMP C2 H F3 O2



REFERENCE COUNT: 67 THERE ARE 67 CITED REFERENCES AVAILABLE FOR  
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L8 ANSWER 9 OF 20 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1999:550813 CAPLUS

DOCUMENT NUMBER: 131:331365

TITLE: Technetium Complexes of a Hydrazinonicotinamide-Conjugated Cyclic Peptide and 2-Hydrazinopyridine: Synthesis and Characterization. [Erratum to document cited in CA130:346352]

AUTHOR(S): Liu, Shuang; Edwards, D. Scott; Harris, Anthony R.; Heminway, Stuart J.; Barrett, John A.

CORPORATE SOURCE: Medical Imaging Division, DuPont Pharmaceuticals Company, North Billerica, MA, 01862, USA

SOURCE: Inorganic Chemistry (1999), 38(19), 4372

CODEN: INOCAJ; ISSN: 0020-1669

PUBLISHER: American Chemical Society

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The paper by D. J. Rose and co-workers (Inorg. Chem. 1998, 37, 2701-2716) was inadvertently omitted as a ref.

IT 191276-67-2

RL: RCT (Reactant); RACT (Reactant or reagent)

(prepn. of technetium-hydrazinonicotinamide complexes conjugated to cyclic peptides (Erratum))

RN 191276-67-2 CAPLUS

CN Cyclo[N2-methyl-L-arginylglycyl-L-.alpha.-aspartyl-3-(aminomethyl)-5-[[6-[[6-hydrazino-3-pyridinyl]carbonyl]amino]-1-oxohexyl]amino]benzoyl-D-valyl], bis(trifluoroacetate) (9CI) (CA INDEX NAME)

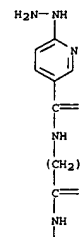
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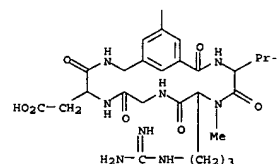
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L8 ANSWER 9 OF 20 CAPLUS COPYRIGHT 2002 ACS (Continued)

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PAGE 2-A



CM 2

CRN 76-05-1

CMF C2 H F3 O2

L8 ANSWER 9 OF 20 CAPLUS COPYRIGHT 2002 ACS (Continued)



L8 ANSWER 10 OF 20 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1999:143289 CAPLUS

DOCUMENT NUMBER: 130:346352

TITLE: Technetium Complexes of a Hydrazinonicotinamide-Conjugated Cyclic Peptide and 2-Hydrazinopyridine: Synthesis and Characterization

AUTHOR(S): Liu, Shuang; Edwards, D. Scott; Harris, Anthony R.; Heminway, Stuart J.; Barrett, John A.

CORPORATE SOURCE: Medical Imaging Division, DuPont Pharmaceuticals Company, North Billerica, MA, 01862, USA

SOURCE: Inorganic Chemistry (1999), 38(6), 1326-1335

CODEN: INOCAJ; ISSN: 0020-1669

PUBLISHER: American Chemical Society

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Ternary ligand technetium complexes of a hydrazinonicotinamide-conjugated cyclic peptide [HYNICtide: cyclo[D-Val-NMeArg-Gly-Asp-Mamb[5-(6-(6-hydrazinonicotinamido)hexanamide]]]) and 2-hydrazinopyridine (HYPY) were prepd. and characterized by various spectroscopic methods. The HPLC concordance expts. for 99mTc and 99Tc analogs show clearly that the same complexes are prepd. on the no-carrier-added (99mTc) and the carrier-added

(99Tc) levels. Using a chirality expt., it was demonstrated that the presence of two radiometric peaks in the HPLC chromatograms of RP444, RP445, and RP446 is due to the resoln. of diastereomers, which result

from the presence of chiral cyclic peptide and the formation of two enantiomers

of the technetium chelate. In a ligand challenge expt., it was found that

the high soln. stability of these ternary ligand [99mTc]HYNICtide complexes is due to their kinetic inertness. The 1:1:1:1 compn. for Tc:HYNICtide:tricine (L = TPPTS, TPPDS, and TPMS) in these ternary ligand [99Tc]HYNICtide complexes is confirmed by 1H NMR and FAB mass spectral data and is completely consistent with that detd. on the tracer (99mTc) level. In addn., the IC50 values of RP444, RP445, and RP446 and the two isomeric forms of RP444 were detd. using a platelet 11b/IIIa binding assay. Both isomeric forms of RP444 were found to have the same binding affinity (IC50 = 13 +/- 2 nM). Complexes [99Tc(HYPY)(PPh3)2Cl2] and [99Tc(HYPY)(PPh3)(tricine)] were isolated from the reaction of HYPY with [n-Bu4N][TcOCl4] in the presence of excess tricine and triphenylphosphine. [99Tc(HYPY)(PPh3)(tricine)] serves as a model for ternary ligand [99mTc]HYNICtide complexes. Both complexes have been characterized by HPLC, spectroscopic (IR, NMR, and FAB-MS) methods, and elemental anal. The HPLC concordance for complexes [99mTc(HYPY)(PPh3)(tricine)] and [99Tc(HYPY)(PPh3)(tricine)] shows that the two complexes are identical. The NMR (1H and 13C) data suggests that the complex [99Tc(HYPY)(PPh3)(tricine)] has an octahedral coordination geometry with a monodentate diazenido HYPY, a tetradentate tricine, and a monodentate triphenylphosphine co-ligand.

IT 191276-67-2

RL: RCT (Reactant); RACT (Reactant or reagent)

(prepn. of technetium-hydrazinonicotinamide complexes conjugated to cyclic peptides)

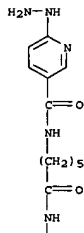
RN 191276-67-2 CAPLUS

CN Cyclo[N2-methyl-L-arginylglycyl-L-.alpha.-aspartyl-3-(aminomethyl)-5-[[6-[[6-hydrazino-3-pyridinyl]carbonyl]amino]-1-oxohexyl]amino]benzoyl-D-valyl], bis(trifluoroacetate) (9CI) (CA INDEX NAME)

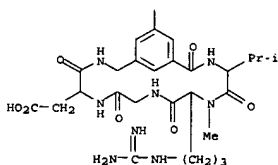
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L8 ANSWER 10 OF 20 CAPLUS COPYRIGHT 2002 ACS (Continued)  
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 CMP C38 H55 N13 O9

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CM 2  
 CRN 76-05-1  
 CMP C2 H F3 O2

L8 ANSWER 10 OF 20 CAPLUS COPYRIGHT 2002 ACS (Continued)

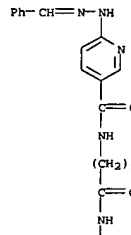


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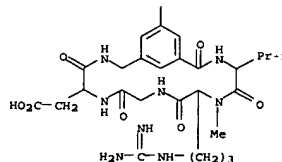
L8 ANSWER 11 OF 20 CAPLUS COPYRIGHT 2002 ACS  
 ACCESSION NUMBER: 1999:436748 CAPLUS  
 DOCUMENT NUMBER: 131:228976  
 TITLE: Synthesis of stable hydrazones of a hydrazinonicotinyl-modified peptide for the preparation of 99mTc-labeled radiopharmaceuticals  
 AUTHOR(S): Harris, Thomas D.; Sworin, Michael; Williams, Neal; Rajopadhye, Milind; Damphousse, Paul R.; Glowacka, Danuta; Poirier, Michael J.; Yu, Karmine  
 CORPORATE SOURCE: DuPont Pharmaceutical Co., North Billerica, MA, 01862, USA  
 SOURCE: Bioconjugate Chemistry (1999), 10(5), 808-814  
 CODEN: BCCHES; ISSN: 1043-1802  
 PUBLISHER: American Chemical Society  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 AB Hydrazones of a 6-hydrazinonicotinyl-modified cyclic peptide IIb/IIia receptor antagonist were prepd. in order to protect the hydrazine moiety from reaction with trace aldehyde and ketone impurities encountered during the process of manuf. and compounding lyophilized kits used in radiolabeling with 99mTc. Hydrazones were prepd. by either a direct reaction of the 6-hydrazinonicotinyl-modified cyclic peptide I with carbonyl compds. or by conjugation of the cyclic peptide with hydrazones of succinimidyl 6-hydrazinonicotinate II (R1 = Ph, CH2Ph, CH2OH, C6H4NMe2-4, C6H4CO2H-4, C6H4SO3Na-2, CH3CHCH3, CO2H, etc.; R2 = H). Stability of the hydrazones was evaluated by treatment with formaldehyde. Hydrazones derived from simple aliph. aldehydes underwent an exchange reaction with formaldehyde, while hydrazones of arom. aldehydes and ketones provided the greatest level of stability when challenged with formaldehyde. The authors have been successful in protecting 6-hydrazinonicotinyl-modified cyclic peptides from reacting with formaldehyde, while still allowing sufficient reactivity for radiolabeling with 99mTc. The hydrazones of succinimidyl 6-hydrazinonicotinate are convenient as general reagents for forming 6-hydrazinonicotinyl conjugates with amino-functionalized bioactive mols.  
 IT 186304-73-4P 186304-77-8P 186304-78-9P  
 186304-81-4P 186304-83-6P 186304-85-8P  
 186304-93-8P 186305-01-1P 207600-71-3P  
 243965-37-9P 243965-38-0P 243965-39-1P  
 243965-40-4P 243965-41-5P  
 RL: PEP (Physical, engineering or chemical process); SPN (Synthetic preparation); PREP (Preparation); PROC (Process)  
 (prepn. of stable hydrazone deriva. of hydrazinonicotinyl-cyclopeptides for radiolabeling with 99mTc)  
 RN 186304-73-4 CAPLUS  
 CN Cyclo[N2-methyl-L-arginylglycyl-L-.alpha.-aspartyl-3-(aminomethyl)-5-[[6-[[[6-[(phenylmethylene)hydrazino]-3-pyridinyl]carbonyl]amino]-1-oxohexyl]amino]benzoyl-D-valyl]] (9CI) (CA INDEX NAME)

L8 ANSWER 11 OF 20 CAPLUS COPYRIGHT 2002 ACS (Continued)

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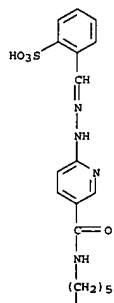


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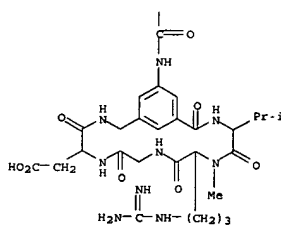


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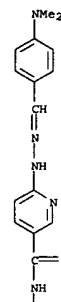
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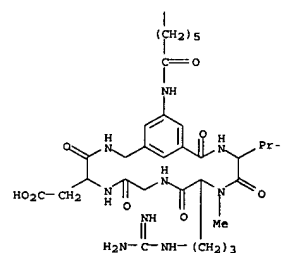
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L8 ANSWER 11 OF 20 CAPLUS COPYRIGHT 2002 ACS (Continued)

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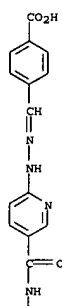
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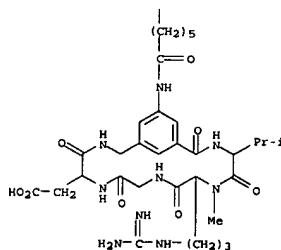
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L8 ANSWER 11 OF 20 CAPLUS COPYRIGHT 2002 ACS (Continued)

PAGE 1-A



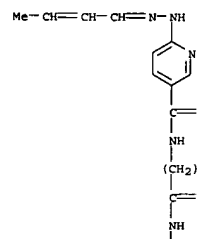
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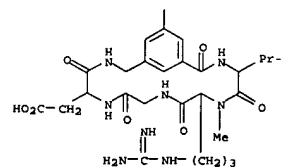
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L8 ANSWER 11 OF 20 CAPLUS COPYRIGHT 2002 ACS (Continued)

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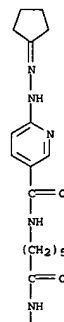
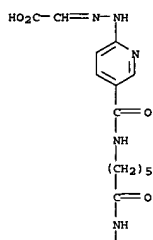


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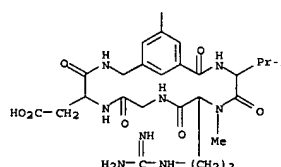
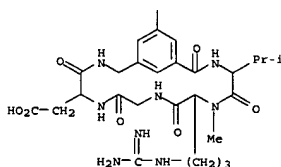


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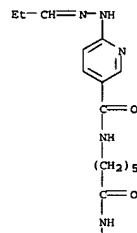
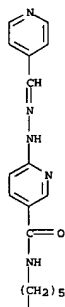


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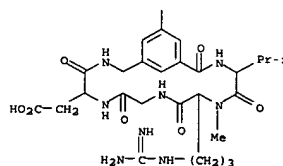
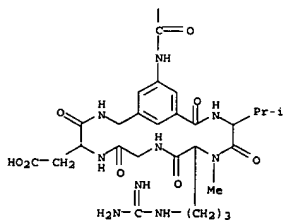
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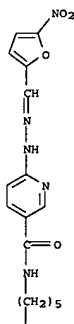
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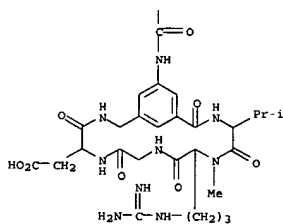
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L8 ANSWER 11 OF 20 CAPLUS COPYRIGHT 2002 ACS (Continued)

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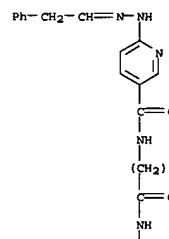
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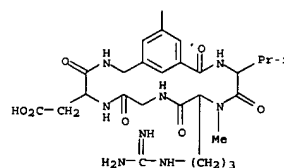
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L8 ANSWER 11 OF 20 CAPLUS COPYRIGHT 2002 ACS (Continued)

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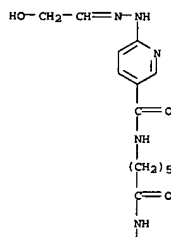
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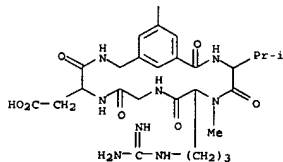
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L8 ANSWER 11 OF 20 CAPLUS COPYRIGHT 2002 ACS (Continued)

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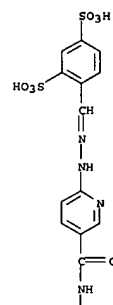
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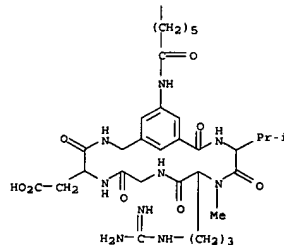
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L8 ANSWER 11 OF 20 CAPLUS COPYRIGHT 2002 ACS (Continued)

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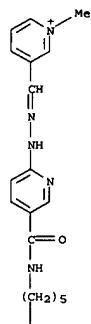


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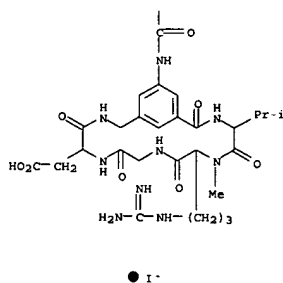
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L8 ANSWER 11 OF 20 CAPLUS COPYRIGHT 2002 ACS (Continued)

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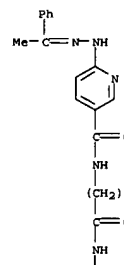


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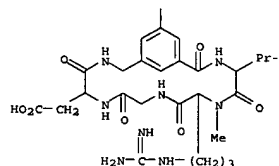
L8 ANSWER 11 OF 20 CAPLUS COPYRIGHT 2002 ACS (Continued)

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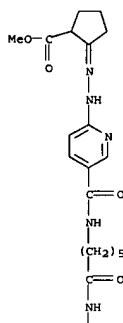


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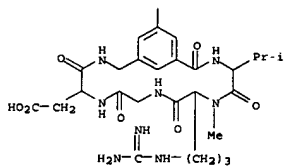
L8 ANSWER 11 OF 20 CAPLUS COPYRIGHT 2002 ACS (Continued)

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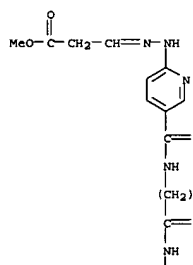
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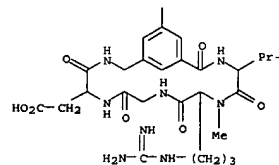
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L8 ANSWER 11 OF 20 CAPLUS COPYRIGHT 2002 ACS (Continued)

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15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR  
 RECORD. ALL CITATIONS AVAILABLE IN THE RE

FORMAT

L8 ANSWER 12 OF 20 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1999:423883 CAPLUS

DOCUMENT NUMBER: 131:233447

TITLE: 99mTc-Labeling of Hydrazones of a  
Hydrazinonicotinamide Conjugated Cyclic Peptide  
AUTHOR(S): Edwards, D. Scott; Liu, Shuang; Harris, Anthony R.;  
Poixier, Michael J.; Ewels, Barbara A.

CORPORATE SOURCE: Medical Imaging Division, DuPont Pharmaceuticals  
Company, North Billerica, MA, 01862, USA

SOURCE: Bioconjugate Chemistry (1999), 10(5), 803-807  
CODEN: BCCHES; ISSN: 1043-1802

PUBLISHER: American Chemical Society

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Eight HYNIC-tide (HYNIC-derivatized cyclic peptide) hydrazones (three with  
aliph. substituents and five with arom. groups) were studied for their  
potential use as the final intermediate for prepn. of RP444, a new  
radiopharmaceutical under development for imaging thrombosis. The goal

of this study is to screen various hydrazones through stability testing and  
radiolabeling and find those which are able to remain stable without  
significant degrdn. in the manufg. process and at the same time are  
reactive to produce enough free hydrazine in situ for successful  
99mTc-labeling. In an initial screening study, only hydrazones which  
contain aliph. substituents gave satisfactory (>90%) yields of  
RP444 using 50 .degree.C and 30 min of heating. However, their soln.  
instability excludes them from being used as com. reagents. Benzaldehyde  
and 2-sulfonatobenzaldehyde-substituted hydrazones gave >90%

yields when the reaction mixts. were heated at 80 .degree.C for 30 min. These  
hydrazones can be used as the final intermediate for prepn. of RP444.

The combination of 40 mg of tricine, 1-10 mg of TPPTS, 20-40 .mu.g of  
hydrazone 1 or 4 for 50 mCi of [99mTc]pertechnetate, 20-50 .mu.g of  
stannous chloride, pH 4.5 +/- 0.5, and heating at 80 .degree.C for 30

min gives the best yield for RP444.

IT 167214-98-4P 186304-73-4P 186304-78-9P

186304-81-4P 186304-83-6P 186304-85-8P

186305-01-1P 186305-30-6P 207600-71-3P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT  
(Reactant or reagent)

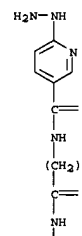
(99mTc-labeling of hydrazones of hydrazinonicotinamide conjugated  
cyclic peptide)

RN 167214-98-4 CAPLUS

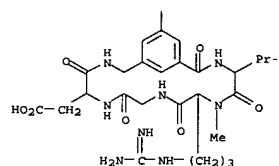
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L8 ANSWER 12 OF 20 CAPLUS COPYRIGHT 2002 ACS (Continued)

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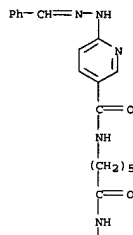


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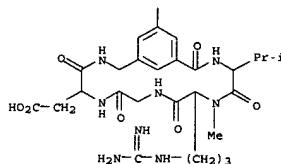
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L8 ANSWER 12 OF 20 CAPLUS COPYRIGHT 2002 ACS (Continued)

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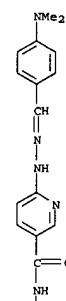


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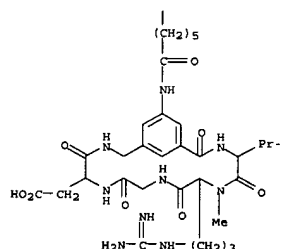
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L8 ANSWER 12 OF 20 CAPLUS COPYRIGHT 2002 ACS (Continued)

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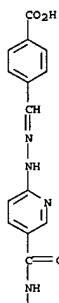


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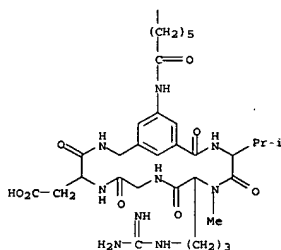
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L8 ANSWER 12 OF 20 CAPLUS COPYRIGHT 2002 ACS (Continued)

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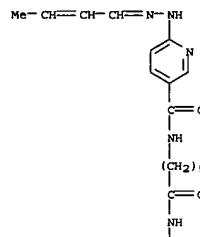
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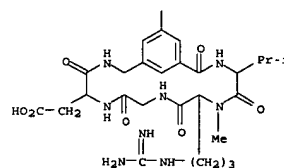
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L8 ANSWER 12 OF 20 CAPLUS COPYRIGHT 2002 ACS (Continued)

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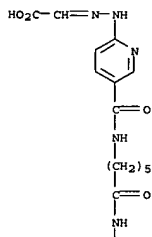
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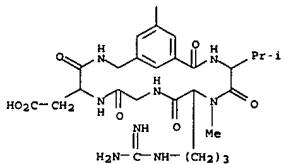
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L8 ANSWER 12 OF 20 CAPLUS COPYRIGHT 2002 ACS (Continued)

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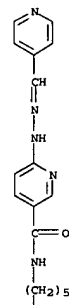
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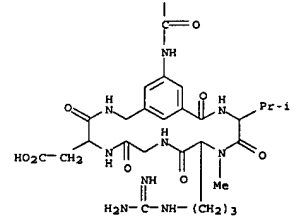
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L8 ANSWER 12 OF 20 CAPLUS COPYRIGHT 2002 ACS (Continued)

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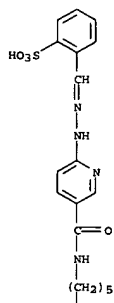
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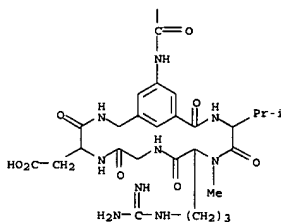
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L8 ANSWER 12 OF 20 CAPLUS COPYRIGHT 2002 ACS (Continued)

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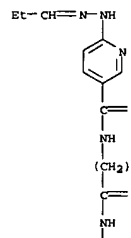


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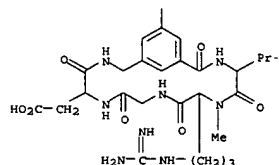
RN 207600-71-3 CAPLUS  
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L8 ANSWER 12 OF 20 CAPLUS COPYRIGHT 2002 ACS (Continued)

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REFERENCE COUNT: 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE REFORMAT

L8 ANSWER 13 OF 20 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 2  
 ACCESSION NUMBER: 1998:331341 CAPLUS  
 DOCUMENT NUMBER: 129:16392  
 TITLE: Preparation of stable hydrazones linked to a peptide moiety as reagents for the preparation of radiopharmaceuticals  
 INVENTOR(S): Sworin, Michael; Rajopadhye, Milind; Harris, Thomas David; Edwards, David Scott; Cheesman, Edward Hollister; Liu, Shuang  
 PATENT ASSIGNEE(S): DuPont Merck Pharmaceutical Co., USA  
 SOURCE: U.S., 34 pp., Cont.-in-part of U.S. Ser. No. 218,861. CODEN: USXXAM  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 6  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5750088	A	19980512	US 1995-476296	19950607
US 5879657	A	19990309	US 1994-218861	19940328
CA 2222183	AA	19961219	CA 1996-2222183	19960607
WO 9640637	A1	19961219	WO 1996-US9766	19960607

W: AM, AT, AU, AZ, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, HU, IL, JP, KG, KR, KZ, LT, LU, LV, MD, MX, NO, NZ, PL, PT, RO, RU, SE, SG, SI, SK, TJ, TM, UA, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
AU 9661661	A1	19961230	AU 1996-61661	19960607
AU 718683	B2	20000420		
ZA 9604854	A	19971208	ZA 1996-4854	19960607
EP 832068	A1	19980401	EP 1996-919289	19960607

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CN 1192733	A	19980909	CN 1996-196141	19960607
JP 11507364	T2	19990629	JP 1996-501990	19960607
BR 9609003	A	19991214	BR 1996-9003	19960607
US 6015904	A	20000118	US 1997-956313	19971023
NO 9705678	A	19980206	NO 1997-5678	19971205
LT 4380	B	19980427	LT 1997-191	19971205
LV 12044	B	19980920	LV 1997-247	19980128

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 US 1994-218861 A2 19940328  
 US 1995-476296 A 19950607  
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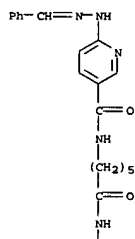
OTHER SOURCE(S): MARPAT 129:16392  
 AB This invention provides novel reagents (Q)pln-Hz [Q = biol. active peptide or peptidomimetic; p = 1-20; Ln = linking group  
 f, [(CH2)g2]g' (CR55R56)g'' [Y1(CR55R56)FY2]f(CR55R56)g'' [Z1(CH2)g]g'; each f', g, g'' = 0-10; each g', f'' = 0, 1; Y1, Y2 = independently bond, O, NR56, CO, CO2, OCO2, CONH, C(NR56), S, S(O), SO2, SO3, NHCO, NHCONH, NHCSNH; each Z1 = (un)substituted, (un)satd. or arom. C6-14 ring; R55, R56 = independently H, (un)substituted C1-10 alkyl, (un)substituted alkaryl; Hz = stable hydrazone group R40R41NN:CR80R81; R40 = bond to Ln, optionally substituted C1-10 alkyl, aryl, cycloalkyl, heterocyclyl, heterocycloalkyl,

L8 ANSWER 13 OF 20 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 2  
 (Continued)  
 or alkaryl; R41 = H, optionally substituted aryl, C1-10 alkyl, or heterocyclyl; R80, R81 = independently H, C1-10 alkyl, CN, CO2R85, COR85, CON(R85)2, optionally substituted C2-10 alkenyl, unsatd. heterocyclyl, unsatd. carbocyclyl; R80R81 = 5-6 membered cycloalkylidene group; R85 = H, C1-6 alkyl, and pharmaceutically acceptable salts thereof, for the prepn. of radiopharmaceuticals useful as imaging agents for the diagnosis of cardiovascular disorders, infection, inflammation and cancer, diagnostic kits comprising said reagents and intermediate compds. useful for the prepn. of said reagents. The reagents are comprised of stable hydrazones modified biol. active mols. that react with gamma emitting radioisotopes to form radiopharmaceuticals that selectively localize at sites of disease and thus allow an image to be obtained of the loci using gamma scintigraphy. Thus, condensation of succinimidyl 6-(2-benzaldehydehydrazino)nicotinate (prepn. given) with an amino-functionalized cyclopeptide gave desired cyclopeptide hydrazone I. I and related hydrazones were radiolabeled with 99mTcO4- to give radiopharmaceutical complexes in 30-94% yields.  
 IT 186304-73-4P 186304-78-9P 186304-81-4P 186304-83-6P 186304-85-8P 186304-87-0P 186304-90-5P 186305-01-1P 186305-30-6P 207600-46-2P 207600-51-9P 207600-53-1P 207600-54-2P  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses) (prepn. of stable hydrazones linked to a peptide moiety as reagents for the prepn. of radiopharmaceuticals)  
 RN 186304-73-4 CAPLUS  
 CN Cyclo(N2-methyl-L-arginylglycyl-L-.alpha.-aspartyl-3-(aminomethyl)-5-[[6-[[[6-(phenylmethylene)hydrazino]-3-pyridinyl]carbonyl]amino]-1-oxohexyl]amino]benzoyl-D-valyl] (9CI) (CA INDEX NAME)

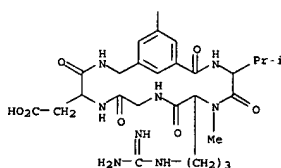
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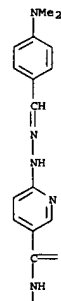


RN 186304-78-9 CAPLUS  
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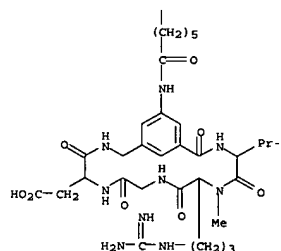
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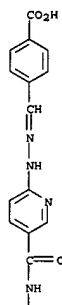
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L8 ANSWER 13 OF 20 CAPLUS COPYRIGHT 2002 ACS  
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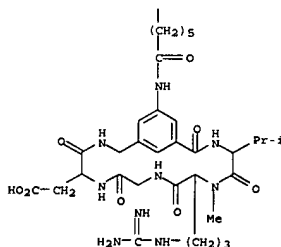
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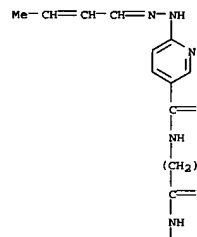


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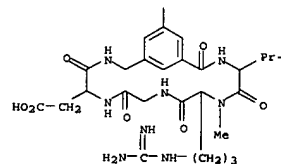
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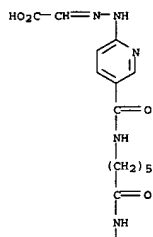
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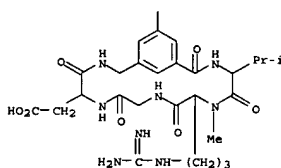
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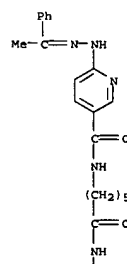


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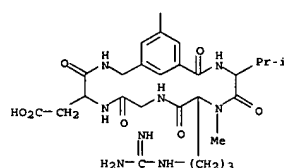
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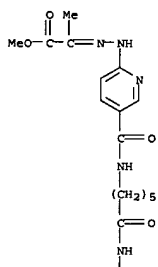


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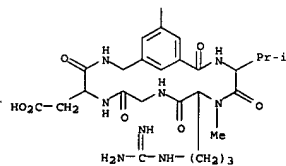
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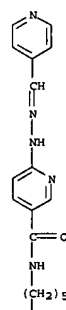


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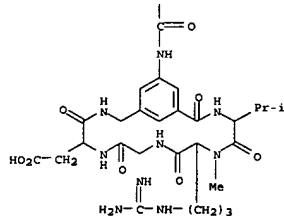
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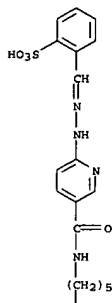


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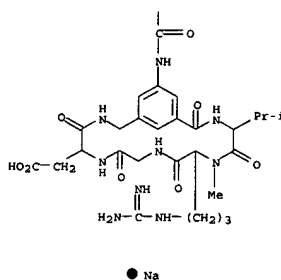
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L8 ANSWER 13 OF 20 CAPLUS COPYRIGHT 2002 ACS  
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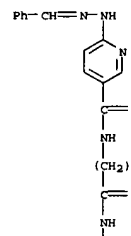
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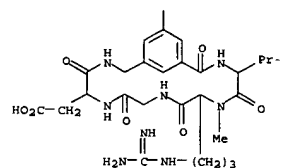
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DUPLICATE 2

CM 2

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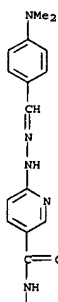


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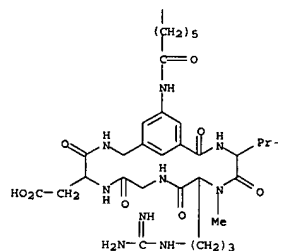
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DUPLICATE 2

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CM 2

CRN 76-05-1  
CMF C2 H F3 O2



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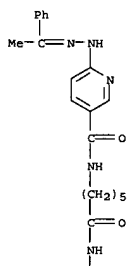
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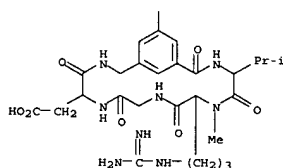
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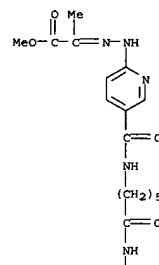


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CRN 186304-90-5  
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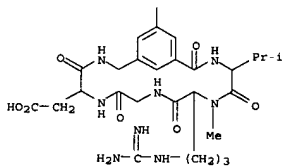


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L8 ANSWER 13 OF 20 CAPLUS COPYRIGHT 2002 ACS  
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DUPLICATE 2

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CM 2

CRN 76-05-1  
CMF C2 H F3 O2

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RL: BAC (Biological activity or effector, except adverse); BSU

(Biological

study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(prepn. of stable hydrazones linked to a peptide moiety as reagents

for

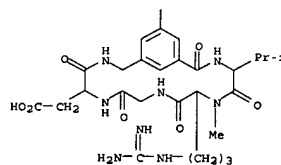
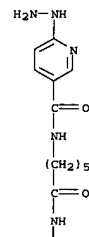
the prepn. of radiopharmaceuticals)

RN 167214-98-4 CAPLUS

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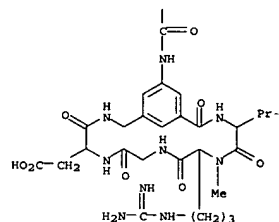
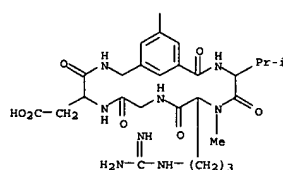
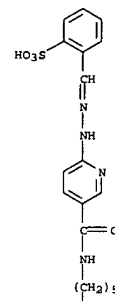
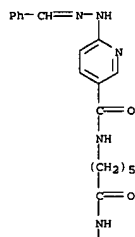
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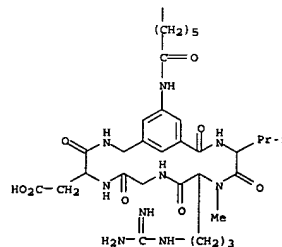
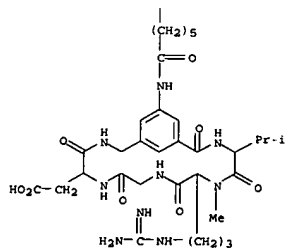
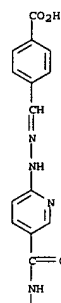
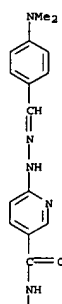
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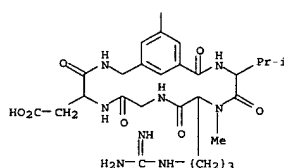
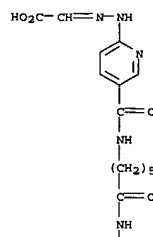
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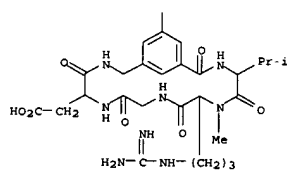
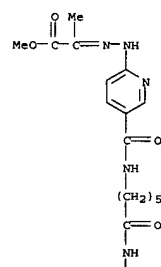
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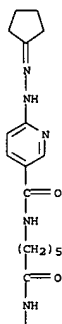


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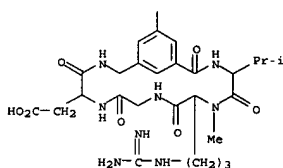
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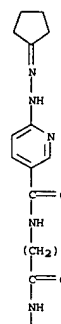


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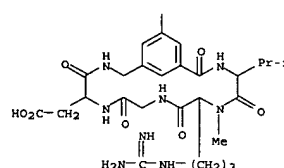
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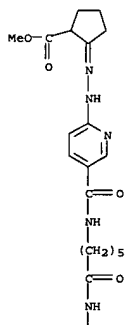


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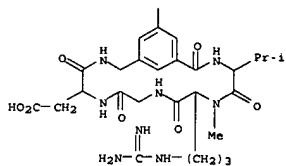
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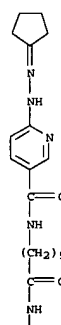
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CRN 186304-93-8  
 CMP C43 H61 N13 O9

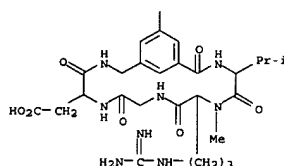
L8 ANSWER 13 OF 20 CAPLUS COPYRIGHT 2002 ACS  
(Continued)

DUPLICATE 2

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CM 2

CRN 76-05-1  
 CMP C2 H F3 O2



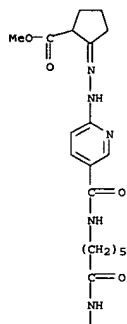
L8 ANSWER 13 OF 20 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 2  
(Continued)

RN 207600-57-5 CAPLUS  
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[[[6-[[2-(methoxycarbonyl)cyclopentylidene]hydrazino]-3-  
pyridinyl]carbonyl]amino]-1-oxohexyl]amino]benzoyl-D-valyl],  
trifluoroacetate (9CI) (CA INDEX NAME)

CM 1

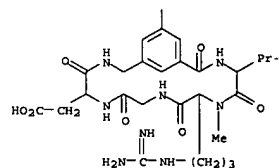
CRN 186304-97-2  
CMP C45 H63 N13 O11

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L8 ANSWER 13 OF 20 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 2  
(Continued)

PAGE 2-A



CM 2

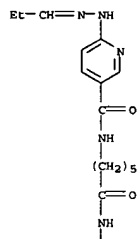
CRN 76-05-1  
CMP C2 H F3 O2



RN 207600-71-3 CAPLUS  
CN Cyclo[N2-methyl-L-arginylglycyl-L-.alpha.-aspartyl-3-(aminomethyl)-5-[[1-  
oxo-6-[[[6-(propylidenehydrazino)-3-pyridinyl]carbonyl]amino]hexyl]amino]b  
enzoyl-D-valyl] (9CI) (CA INDEX NAME)

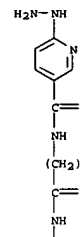
L8 ANSWER 13 OF 20 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 2  
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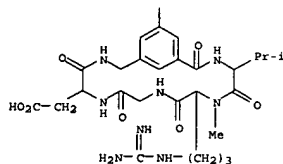


L8 ANSWER 13 OF 20 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 2  
(Continued)

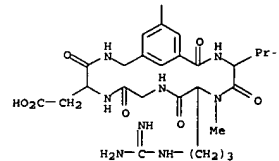
PAGE 1-A



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IT 167214-98-4 207600-66-6  
RL: RCT (Reactant); RACT (Reactant or reagent)  
(prepn. of stable hydrazones linked to a peptide moiety as reagents  
for

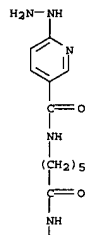
the prepn. of radiopharmaceuticals)  
RN 167214-98-4 CAPLUS  
CN Cyclo[3-(aminomethyl)-5-[[6-[[[6-hydrazino-3-pyridinyl]carbonyl]amino]-1-  
oxohexyl]amino]benzoyl-D-valyl-N2-methyl-L-arginylglycyl-L-.alpha.-  
aspartyl] (9CI) (CA INDEX NAME)

RN 207600-66-6 CAPLUS  
CN Cyclo[N2-methyl-L-arginylglycyl-L-.alpha.-aspartyl-3-(aminomethyl)-5-[[6-  
[[[6-hydrazino-3-pyridinyl]carbonyl]amino]-1-oxohexyl]amino]benzoyl-D-  
valyl], dihydrobromide (9CI) (CA INDEX NAME)

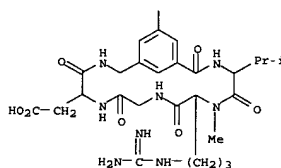
L8 ANSWER 13 OF 20 CAPLUS COPYRIGHT 2002 ACS  
(Continued)

DUPLICATE 2

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● 2 HBr

L8 ANSWER 14 OF 20 CAPLUS COPYRIGHT 2002 ACS  
(Continued)

DUPLICATE 3

[99mTc(tricine) (TPPTS) (L)] [H<sub>2</sub>L = 1, TPPTS = tris(3-sulfonatophenyl)phosphine, sodium salt] was prepd. in 95% yield.

IT 167214-98-4

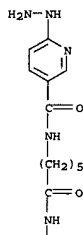
RL: RCT (Reactant); RACT (Reactant or reagent)

(for prepn. of technetium-99m tricine phosphine complexes with cyclic peptide ligands as imaging agents for diagnosis of cardiovascular disorders, infectious disease and cancer)

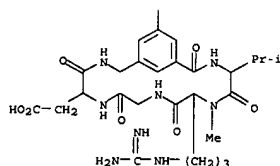
RN 167214-98-4 CAPLUS

CN Cyclo[3-(aminomethyl)-5-[[6-[(6-hydrazino-3-pyridinyl)carbonyl]amino]-1-oxohexyl]amino]benzoyl-D-valyl-L-arginylglycyl-L-α-aspartyl (9CI) (CA INDEX NAME)

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L8 ANSWER 14 OF 20 CAPLUS COPYRIGHT 2002 ACS

DUPLICATE 3

ACCESSION NUMBER: 1998:277219 CAPLUS  
DOCUMENT NUMBER: 128:330389  
TITLE: Ternary radiopharmaceutical complexes  
INVENTOR(S): Edwards, David Scott; Liu, Shuang  
PATENT ASSIGNEE(S): DuPont Merck Pharmaceutical Co., USA  
SOURCE: U.S., 27 pp., Cont.-in-part of U.S. Ser. No. 218,861.  
CODEN: USXXAM  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 6  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5744120	A	19980428	US 1995-415908	19950403
US 5879657	A	19990309	US 1994-218861	19940328
CA 2216423	AA	19961010	CA 1996-2216423	19960403
WO 9631243	A1	19961010	WO 1996-US4567	19960403
W: AU, BR, CA, CN, CZ, EE, HU, JP, KR, LT, LV, MX, NO, NZ, PL, RO, SG, SI, SK, UA, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
AU 9657874	A1	19961023	AU 1996-57874	19960403
AU 719529	B2	20000511		
ZA 9602672	A	19971003	ZA 1996-2672	19960403
EP 820312	A1	19980128	EP 1996-914548	19960403
EP 820312	B1	20020710		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
CN 1185116	A	19980617	CN 1996-194172	19960403
CN 1080127	B	20020306		
JP 11503166	T2	19990323	JP 1996-530453	19960403
BR 9608065	A	19990629	BR 1996-8065	19960403
EP 1195168	A2	20020410	EP 2001-123928	19960403
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
LV 12039	B	19981020	LV 1997-185	19971001
LT 4391	B	19981026	LT 1997-157	19971001
NO 9704549	A	19971202	NO 1997-4549	19971002
US 6010679	A	20000104	US 1998-13320	19980126
PRIORITY APPLN. INFO.:				
		US 1993-40336	B2	19930330
		US 1994-218861	A2	19940328
		US 1995-415908	A	19950403
		EP 1996-914548	A3	19960403
		WO 1996-US4567	W	19960403

OTHER SOURCE(S): MARPAT 128:330389  
AB This invention provides novel radiopharmaceuticals which are useful as imaging agents for the diagnosis of cardiovascular disorders, infectious disease and cancer. The radiopharmaceuticals are comprised of phosphine or arsine ligated technetium-99m labeled hydrazino or diazino modified biol. active mols. that selectively localize at sites of disease and thus allow an image to be obtained of the loci using gamma scintigraphy. This invention also provides methods for using the radiopharmaceuticals and kits comprising radiopharmaceutical precursors. The radiopharmaceuticals of this invention have the structure: [(Q'd'Ln-Ch')xMC(AlI)]y(AL2)z; wherein the variables are as defined herein. Thus,

L8 ANSWER 15 OF 20 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1998:513060 CAPLUS  
DOCUMENT NUMBER: 129:287348  
TITLE: A Novel Ternary Ligand System for 99mTc-Labeling of Hydrazino Nicotinamide-Modified Biologically Active Molecules Using Imine-N-Containing Heterocycles as Coligands  
AUTHOR(S): Liu, Shuang; Edwards, D. Scott; Harris, Anthony R.  
CORPORATE SOURCE: Radiopharmaceuticals Division, The DuPont Merck Pharmaceutical Company, North Billerica, MA, 01862, USA  
SOURCE: Bioconjugate Chemistry (1998), 9(5), 583-595  
CODEN: BCCHES; ISSN: 1043-1802  
PUBLISHER: American Chemical Society  
DOCUMENT TYPE: Journal  
LANGUAGE: English  
AB A hydrazinonicotinamide-functionalized cyclic platelet glycoprotein 11b/11la (GPIIb/11la) receptor antagonist [HYNICtide, cyclo(D-Val-NMeArg-Gly-Asp-Mamb(5-[6-(6-hydrazinonicotinamido)hexanamide)])] was labeled with 99mTc using tricine and a series of imine-N-contg. heterocycles as coligands. The imine-N-contg. heterocycles include N-omega-Acetylhistamine (HIS-AC), N-(2-hydroxyethyl)isonicotinamide (ISONIC-HE), isonicotinic acid (ISONIC), isonicotinoyl-L-aspartic acid di-Me ester (ISONIC-L-Asp-OMe2), 4-methyl-5-thiazolethanol (MTE), nicotinic acid (NIC), 3-nitro-1,2,4-triazole (NTZ), 4-pyridylacetic acid (PA), 4-pyridinesulfonic acid (PES), and 3-pyridinesulfonic acid (PSA). The synthesis of these new ternary ligand [99mTc]HYNICtide complexes can be performed in one or two steps in high yield and high specific activity (.gtoreq.10 000 Ci/mmol HYNICtide). For example, the reaction of HYNICtide, [99mTc]pertechnetate, nicotinic acid, stannous chloride, and tricine at pH .apprx.5 and 100.degree. for 20 min results in the complex [99mTc(HYNICtide)(tricine)(NIC)] in .gtoreq.90% yield as detd. by radio-HPLC. It was found that ternary ligand technetium complexes, [99mTc(HYNICtide)(tricine)(L)] (L = ISONIC, ISONIC-L-Asp-OMe2, ISONIC-HE, MTE, PA, PES, and PSA) are formed as equal mixts. of two isomeric forms. Complex [99mTc(HYNICtide)(tricine)(L)] (L = HIS-AC and NTZ) showed more than two well-resolved radiometric peaks at the retention times of interest, suggesting that they may have more than two forms in soln. due to different bonding modalities of HIS-AC and NTZ. By a chirality expt., it was found that the presence of two radiometric peaks is a result of the

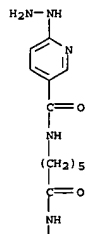
the resolu. of the two diastereomers which are formed by the combination of the chiral HYNICtide and the chiral technetium chelate. The formation of two diastereomers was also obad. when a chiral imine-N-contg. coligand was used for the radiolabeling of HYNIC-BA. The new ternary ligand [99mTc]HYNICtide complexes were found to be stable for up to 6 h in the reaction mixt. The high soln. stability is attributed to their kinetic inertness. The compn. of these complexes was detd. to be 1:1:1 for Tc:HYNICtide:peptide (L = imine-N-contg. heterocycles) through a series of mixed ligand expts. on the tracer (99mTc) level. The lipophilicity of the ternary ligand [99mTc]HYNICtide complexes can be systematically varied by the choice of polyaminocarboxylate and imine-N-contg. coligands. Using the combination of tricine and an imine-N-contg. coligand, HYNIC-derivatized peptides or other small mols. can be labeled with 99mTc in high specific activity and high stability for potential use as radiopharmaceuticals.

IT 167214-98-4

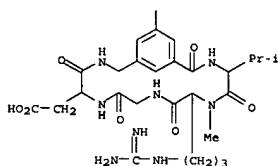


L8 ANSWER 15 OF 20 CAPLUS COPYRIGHT 2002 ACS (Continued)  
 RL: RCT (Reactant); RACT (Reactant or reagent)  
 (a novel ternary ligand system for <sup>99m</sup>Tc-labeling of hydrazino  
 nicotinamide-modified biol. active mols. using imine-N-contg.  
 heterocycles as coliganda)  
 RN 167214-98-4 CAPLUS  
 CN Cyclo[3-(aminomethyl)-5-[[6-[[[6-hydrazino-3-pyridinyl]carbonyl]amino]-1-  
 oxohexyl]amino]benzoyl-D-valyl-N2-methyl-L-arginylglycyl-L-.alpha.-  
 aspartyl] (9CI) (CA INDEX NAME)

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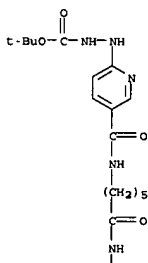


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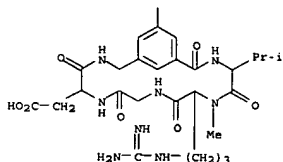


L8 ANSWER 16 OF 20 CAPLUS COPYRIGHT 2002 ACS (Continued)

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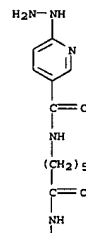
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 CRN 76-05-1  
 CMF C2 H F3 O2



L8 ANSWER 16 OF 20 CAPLUS COPYRIGHT 2002 ACS  
 ACCESSION NUMBER: 1997:330877 CAPLUS  
 DOCUMENT NUMBER: 127:66129  
 TITLE: Synthesis, evaluation and Tc-99m complexation of a  
 hydrazinonicotinyl conjugate of a GP IIb/IIIa  
 antagonist cyclic peptide for the detection of deep  
 vein thrombosis  
 AUTHOR(S): Rajopadhye, Milind; Harris, Thomas D.; Yu, Karmine;  
 Glowacka, Danuta; Damphousse, Paul R.; Barrett, John  
 A.; Heminway, Stuart J.; Edwards, D. Scott; Carroll,  
 Timothy R.  
 CORPORATE SOURCE: Discovery, Radiopharmaceutical Division, The DuPont  
 Merck Pharmaceutical Company, N. Billerica, MA,  
 01862,  
 USA  
 SOURCE: Bioorganic & Medicinal Chemistry Letters (1997),  
 7(8),  
 955-960  
 CODEN: BMCLE8; ISSN: 0960-894X  
 PUBLISHER: Elsevier  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 AB A cyclic peptide GP IIb/IIIa receptor antagonist contg. the  
 'Me-Arg-Gly-Asp' motif has been derivatized with the technetium chelating  
 hydrazinonicotinyl group (Hynic). The Hynic deriv. I and its Tc99  
 diazenido complex, retain the high receptor affinity of the parent  
 peptide. The Tc99 complex shows high thrombus uptake, and rapid  
 clearance  
 of background, producing excellent images in under 1 h.  
 IT 167215-94-39  
 RL: BAC (Biological activity or effector, except adverse); BSU  
 (Biological  
 study, unclassified); RCT (Reactant); SPN (Synthetic preparation); BIOL  
 (Biological study); PREP (Preparation); RACT (Reactant or reagent)  
 (prepn. of Tc99-labeled arginylglycylaspartic acid-contg.  
 cyclopeptides)  
 RN 167215-94-3 CAPLUS  
 CN Cyclo[3-(aminomethyl)-5-[[6-[[[6-[[2-[[1,1-  
 dimethylethoxy]carbonyl]hydrazino]-3-pyridinyl]carbonyl]amino]-1-  
 oxohexyl]amino]benzoyl]-D-valyl-N2-methyl-L-arginylglycyl-, cyclic  
 (41.fwdarw.1)-peptide, mono(trifluoroacetate) (9CI) (CA INDEX NAME)  
 CM 1  
 CRN 167215-93-2  
 CMF C43 H63 N13 O11

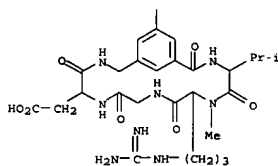
L8 ANSWER 16 OF 20 CAPLUS COPYRIGHT 2002 ACS (Continued)  
 IT 191276-67-2P  
 RL: BAC (Biological activity or effector, except adverse); BSU  
 (Biological  
 study, unclassified); SPN (Synthetic preparation); BIOL (Biological  
 study); PREP (Preparation)  
 (prepn. of Tc99-labeled arginylglycylaspartic acid-contg.  
 cyclopeptides)  
 RN 191276-67-2 CAPLUS  
 CN Cyclo[N2-methyl-L-arginylglycyl-L-.alpha.-aspartyl-3-(aminomethyl)-5-[[6-  
 [[[6-hydrazino-3-pyridinyl]carbonyl]amino]-1-oxohexyl]amino]benzoyl-D-  
 valyl], bis(trifluoroacetate) (9CI) (CA INDEX NAME)  
 CM 1  
 CRN 167214-98-4  
 CMF C38 H55 N13 O9

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L8 ANSWER 16 OF 20 CAPLUS COPYRIGHT 2002 ACS (Continued)

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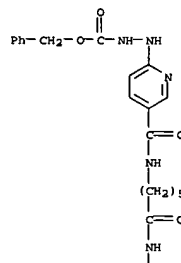


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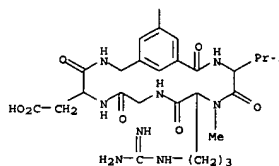
CRN 76-05-1  
CMP C2 H F3 O2

IT 191276-64-9P 191276-66-1P  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT  
 (Reactant or reagent)  
 (prepn. of Tc99-labeled arginylglycylaspartic acid-contg.  
 cyclopeptides)  
 RN 191276-64-9 CAPLUS  
 CN Cyclo[N2-methyl-L-arginylglycyl-L-.alpha.-aspartyl-3-(aminomethyl)-5-[[[1-oxo-6-[[[6-[2-[(phenylmethoxy)carbonyl]hydrazino]-3-pyridinyl]carbonyl]amino]hexyl]amino]benzoyl-D-valyl], mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

CRN 191276-63-8  
CMP C46 H61 N13 O11

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CM 2

CRN 76-05-1  
CMP C2 H F3 O2

L8 ANSWER 16 OF 20 CAPLUS COPYRIGHT 2002 ACS (Continued)

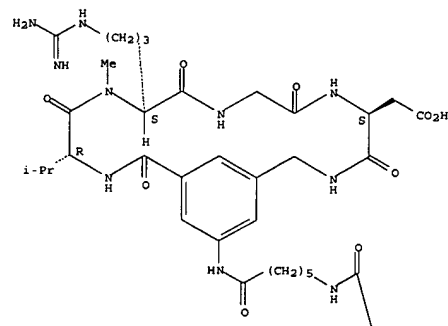


RN 191276-66-1 CAPLUS  
 CN Cyclo[N2-methyl-L-arginylglycyl-L-.alpha.-aspartyl-3-(aminomethyl)-5-[[[6-[[[6-[2-[(9H-fluoren-9-ylmethoxy)carbonyl]hydrazino]-3-pyridinyl]carbonyl]amino]-1-oxohexyl]amino]benzoyl-D-valyl], mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

CRN 191276-65-0  
CMP C53 H65 N13 O11

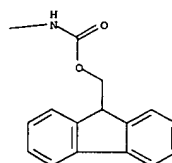
Absolute stereochemistry.



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L8 ANSWER 16 OF 20 CAPLUS COPYRIGHT 2002 ACS (Continued)

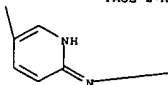
PAGE 2-B



CM 2

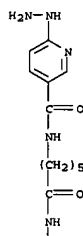
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CMP C2 H F3 O2

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L8 ANSWER 17 OF 20 CAPLUS COPYRIGHT 2002 ACS  
 ACCESSION NUMBER: 1997:536334 CAPLUS  
 DOCUMENT NUMBER: 127:217097  
 TITLE: Literature highlights - 45. 99mTc-labeling of hydrazinonicotinamide (HYNIC) modified highly potent small molecules: problems and solutions  
 AUTHOR(S): Edwards, D. Scott; Liu, Shuang  
 CORPORATE SOURCE: The DuPont Merck Pharmaceutical Company, Radiopharmaceuticals Division, North Billerica, MA, 01862, USA  
 SOURCE: Transition Metal Chemistry (London) (1997), 22(4), 425-426  
 CODEN: TMCHDN; ISSN: 0340-4285  
 PUBLISHER: Chapman & Hall  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 AB The labeling of HYNIC with 99mTc is described for thrombus imaging.  
 IT 167214-98-4  
 RL: RCT (Reactant); RACT (Reactant or reagent)  
 (reactant; 99mTc-labeling of hydrazinonicotinamide-modified small mole.  
 for thrombus imaging)  
 RN 167214-98-4 CAPLUS  
 CN Cyclo[3-(aminomethyl)-5-[[[6-[[[6-hydrazino-3-pyridinyl]carbonyl]amino]-1-oxohexyl]amino]benzoyl-D-valyl-N2-methyl-L-arginylglycyl-L-.alpha.-aspartyl] (9CI) (CA INDEX NAME)

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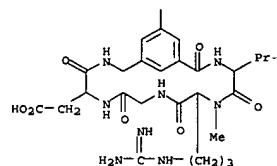
L8 ANSWER 18 OF 20 CAPLUS COPYRIGHT 2002 ACS  
 ACCESSION NUMBER: 1997:116572 CAPLUS  
 DOCUMENT NUMBER: 126:118209  
 TITLE: Stable peptide derivatives for the preparation of radiopharmaceuticals  
 INVENTOR(S): Sworin, Michael; Rajopadhye, Milind; Harris, Thomas David; Edwards, David Scott; Cheesman, Edward Hollister; Liu, Shuang  
 Du Pont Merck Pharmaceutical Company, USA  
 PATENT ASSIGNEE(S): PCT Int. Appl., 114 pp.  
 SOURCE: CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 6  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9640637	A1	19961219	WO 1996-US9766	19960607
W: AM, AT, AU, AZ, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, HU, IL, JP, KG, KR, KZ, LT, LU, LV, MD, MX, NO, NZ, PL, PT, RO, RU, SE, SG, SI, SK, TJ, TM, UA, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
US 5750088	A	19980512	US 1995-476296	19950607
AU 9661661	A1	19961230	AU 1996-61661	19960607
AU 718683	B2	20000420		
EP 832068	A1	19980401	EP 1996-919289	19960607
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI				
JP 11507364	T2	19990629	JP 1996-501990	19960607
BR 9609003	A	19991214	BR 1996-9003	19960607
NO 9705678	A	19980206	NO 1997-5678	19971205
PRIORITY APPLN. INFO.: US 1995-476296 A 19950607				
US 1993-40336 B2 19930330				
US 1994-218861 A2 19940328				
WO 1996-US9766 W 19960607				

OTHER SOURCE(S): MARPAT 126:118209  
 AB Novel reagents for the prepn. of radiopharmaceuticals comprise a biol. active group connected to a stable hydrazone group, optionally via a linking group. The biol. active mol. is selected from IIb/IIia receptor antagonists, IIb/IIia receptor ligands, fibrin binding peptides, leukocyte binding peptides, chemotactic peptides, somatostatin analogs, and selectin binding peptides. The reagents react with gamma emitting radioisotopes to form radiopharmaceuticals that selectively localize at sites of diseases and thus allow an image to be obtained of the loci using gamma scintigraphy. Thus, the benzaldehyde hydrazone of cyclo[D-Val-NMeArg-Gly-Asp-Mamb(hydrazinonicotinyl-5-Ace)] (Mamb = 3-aminomethylbenzoic acid, Aca = aminocaproamide) was prepd. by reaction of cyclo[D-Val-NMeArg-Gly-Mamb(5-Ace)]. 2TPA with succinimidyl 6-(2-benzaldehydehydrazino)nicotinate in DMF at room temp. for 42 h. The product was converted into the 99mTc-based radiopharmaceutical.  
 IT 167214-98-4  
 RL: RCT (Reactant); RACT (Reactant or reagent)

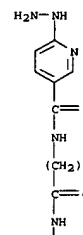
L8 ANSWER 17 OF 20 CAPLUS COPYRIGHT 2002 ACS (Continued)

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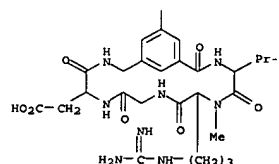


L8 ANSWER 18 OF 20 CAPLUS COPYRIGHT 2002 ACS (Continued)  
 (stable peptide derivs. for the prepn. of radiopharmaceuticals)  
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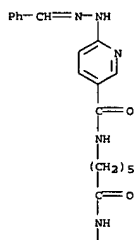
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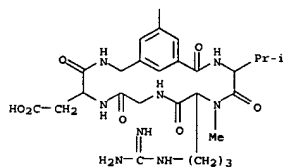
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 186304-88-1P 186304-90-5P 186304-91-6P  
 186305-01-1P 186305-02-2P  
 RL: RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use);  
 BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent);  
 USES (Uses)  
 (stable peptide derivs. for the prepn. of radiopharmaceuticals)

L8 ANSWER 18 OF 20 CAPLUS COPYRIGHT 2002 ACS (Continued)  
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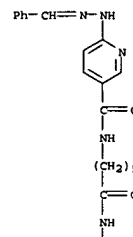
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L8 ANSWER 18 OF 20 CAPLUS COPYRIGHT 2002 ACS (Continued)

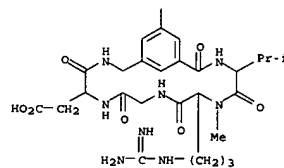
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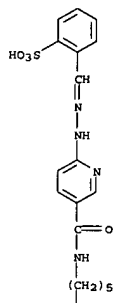
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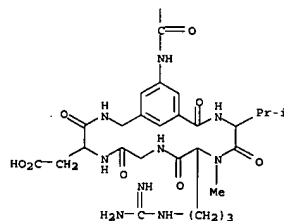
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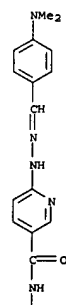
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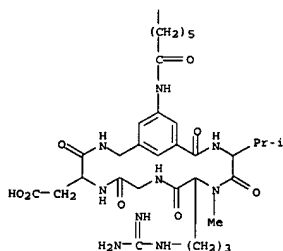
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L8 ANSWER 18 OF 20 CAPLUS COPYRIGHT 2002 ACS (Continued)

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RN 186304-79-0 CAPLUS  
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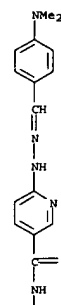
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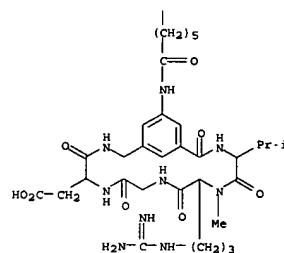
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CM 2

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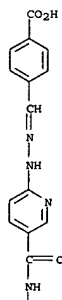
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CMP C2 H3 F3 O2



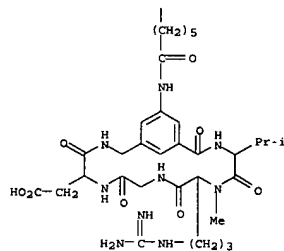
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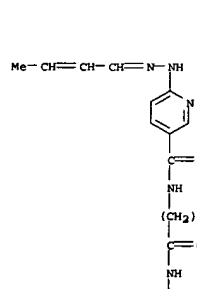
L8 ANSWER 18 OF 20 CAPLUS COPYRIGHT 2002 ACS (Continued)

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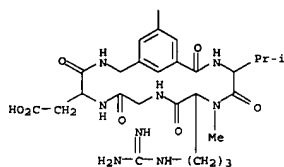
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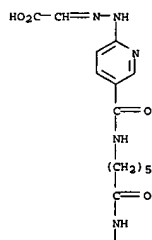
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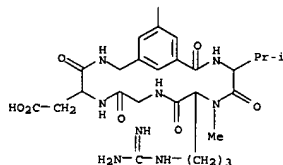
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L8 ANSWER 18 OF 20 CAPLUS COPYRIGHT 2002 ACS (Continued)

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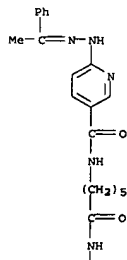


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CM 1

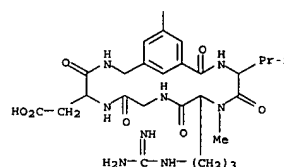
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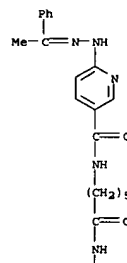
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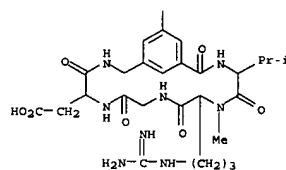
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L8 ANSWER 18 OF 20 CAPLUS COPYRIGHT 2002 ACS (Continued)

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CM 2

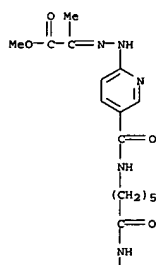
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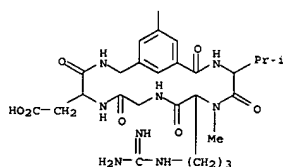
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L8 ANSWER 18 OF 20 CAPLUS COPYRIGHT 2002 ACS (Continued)

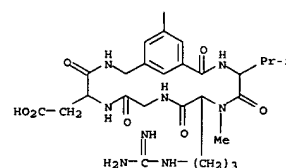
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CM 2

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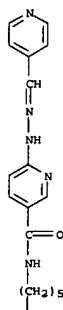
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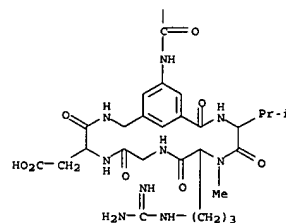
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L8 ANSWER 18 OF 20 CAPLUS COPYRIGHT 2002 ACS (Continued)

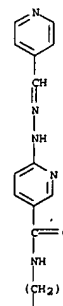


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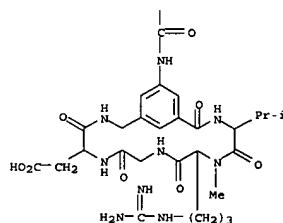
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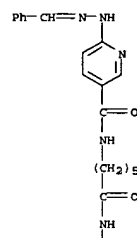
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CMF C2 H F3 O2

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(stable peptide derivs. for the prepn. of radiopharmaceuticals)

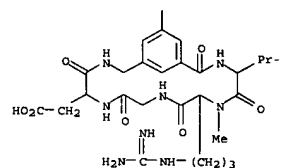
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L8 ANSWER 18 OF 20 CAPLUS COPYRIGHT 2002 ACS (Continued)

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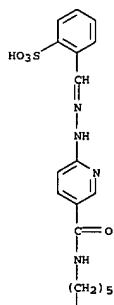
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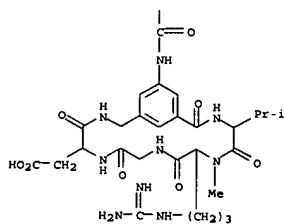
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L8 ANSWER 18 OF 20 CAPLUS COPYRIGHT 2002 ACS (Continued)

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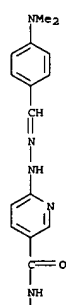
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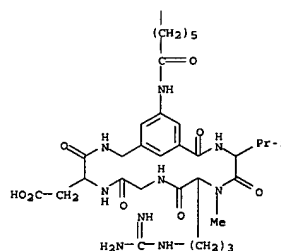
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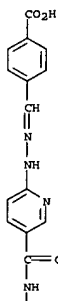


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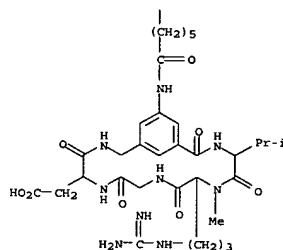


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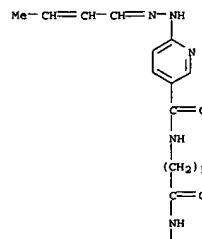
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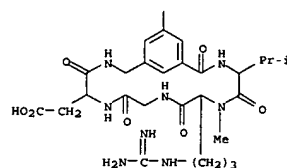
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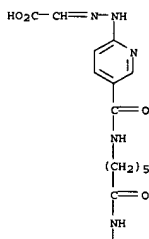
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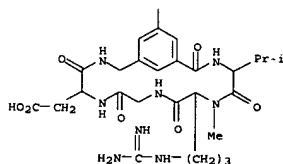
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L8 ANSWER 18 OF 20 CAPLUS COPYRIGHT 2002 ACS (Continued)

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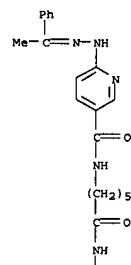
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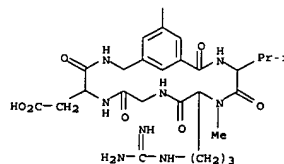
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L8 ANSWER 18 OF 20 CAPLUS COPYRIGHT 2002 ACS (Continued)

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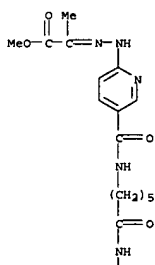
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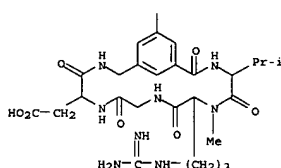
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 INDEX NAME)

L8 ANSWER 18 OF 20 CAPLUS COPYRIGHT 2002 ACS (Continued)

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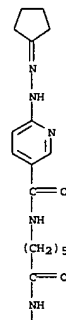
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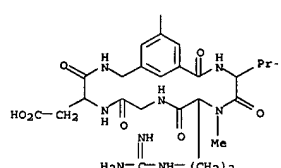
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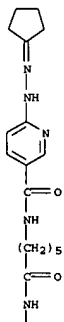
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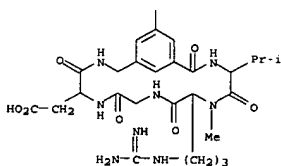
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L8 ANSWER 18 OF 20 CAPLUS COPYRIGHT 2002 ACS (Continued)

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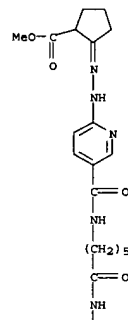
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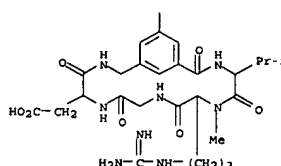


L8 ANSWER 18 OF 20 CAPLUS COPYRIGHT 2002 ACS (Continued)

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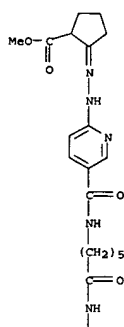
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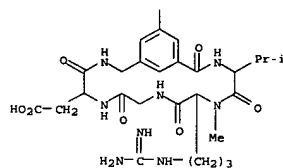
L8 ANSWER 18 OF 20 CAPLUS COPYRIGHT 2002 ACS (Continued)

CRN 186304-97-2  
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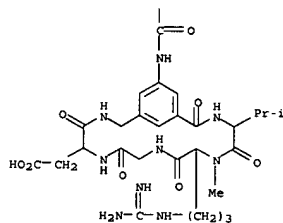


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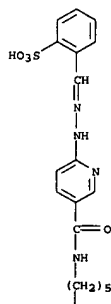
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L8 ANSWER 18 OF 20 CAPLUS COPYRIGHT 2002 ACS (Continued)

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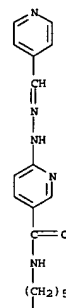
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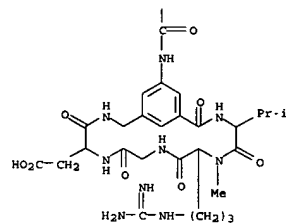
L8 ANSWER 18 OF 20 CAPLUS COPYRIGHT 2002 ACS (Continued)

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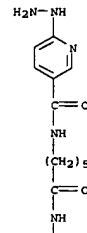


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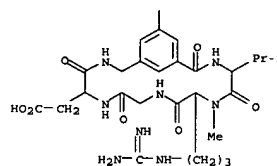
18 ANSWER 19 OF 20 CAPLUS COPYRIGHT 2002 ACS  
 ACCESSION NUMBER: 1996:28281 CAPLUS  
 DOCUMENT NUMBER: 124:49628  
 TITLE: Labeling a Hydrazino Nicotinamide-Modified Cyclic I1b/I11a Receptor Antagonist with 99mTc Using Aminocarboxylates as Coligands  
 AUTHOR(S): Liu, Shuang; Edwards, D. Scott; Looby, Richard J.; Harris, Anthony R.; Poirier, Michael J.; Barrett, John  
 CORPORATE SOURCE: A.; Heminway, Stuart J.; Carroll, Timothy R. Radiopharmaceuticals Division, DuPont Merck Pharmaceutical Company, North Billerica, MA, 01862, USA  
 SOURCE: Bioconjugate Chemistry (1996), 7(1), 63-71  
 CODEN: BCCHE; ISSN: 1043-1802  
 PUBLISHER: American Chemical Society  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 AB A series of 99mTc complexes contg. a hydrazinonicotinamide-conjugated cyclic I1b/I11a receptor antagonist, cyclo(D-Val-NMeArg-Gly-Asp-Mamb-(hydrazinonicotinyl-5-(6-aminocaproic acid))), were synthesized in high yield using tricine or other aminocarboxylates as coligands. These 99mTc complexes have the potential to be used as thrombus imaging agents. The radiolabeling of the HYNIC-conjugated cyclic I1b/I11a peptide (HYNICTide) was carried out by reaction with pertechnetate in the presence of excess tricine and stannous chloride at pH 4-5. The reaction time and temp. depend on the amt. of the HYNICTide and pertechnetate used for the radiolabeling. Very high specific activity (.gtoreq.20 000 mCi/.mu.mol) can be achieved for the complex [99mTc(HYNICTide)(tricine)2] without postlabeling purifi. The complex [99mTc(HYNICTide)(tricine)2] was found by two reversed phase HPLC methods to exist as multiple species, some of which interconvert, depending on the temp., reaction time, and pH of the reaction mixt. The presence of these multiple species is most likely due to different bonding modalities of either the hydrazine moiety of the HYNICTide or the two tricine coligands. The complex [99mTc(HYNICTide)(EDDA)] (EDDA = ethylenediamine-N,N'-diacetic acid) was prepd. either by reacting the cyclic I1b/I11a HYNICTide with pertechnetate, excess EDDA, and stannous chloride at pH 4-5 and 75.degree. for 30 min or by reacting excess EDDA with [99mTc(HYNICTide)(tricine)2]. The complex [99mTc(HYNICTide)(EDDA)] was stable for at least 12 h in the reaction mixt. Three major species were detected in the radio-HPLC chromatograms, presumably due to the more limited no. of possible coordination isomers. Similar results were obtained using other polydentate aminocarboxylates (such as HEDTA, N-(2-hydroxyethyl)ethylenediaminetriacetic acid) as coligands. It is clear that the replacement of tricine by other polydentate aminocarboxylates produces 99mTc-HYNICTide complexes with higher stability and fewer coordination isomers.  
 IT 167214-98-4DP, conjugates with technetium-99m and aminocarboxylate coligands  
 RL: SPN (Synthetic preparation); PREP (Preparation)  
 (labeling a hydrazino nicotinamide-modified cyclic I1b/I11a receptor antagonist with 99mTc using aminocarboxylates as coligands)  
 RN 167214-98-4 CAPLUS  
 CN Cyclo[3-(aminomethyl)-5-[[6-[[[6-hydrazino-3-pyridinyl]carbonyl]amino]-1-oxohexyl]amino]benzoyl-D-valyl-L-methyl-L-arginylglycyl-L-.alpha.-

18 ANSWER 19 OF 20 CAPLUS COPYRIGHT 2002 ACS (Continued)  
 aspartyl] (9CI) (CA INDEX NAME)

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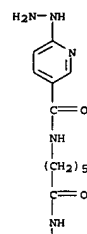
18 ANSWER 20 OF 20 CAPLUS COPYRIGHT 2002 ACS  
 ACCESSION NUMBER: 1996:767392 CAPLUS  
 DOCUMENT NUMBER: 123:199405  
 TITLE: Preparation of radiolabeled platelet GPIIb/IIIa receptor antagonists as imaging agents for the diagnosis of thromboembolic disorders.  
 INVENTOR(S): DeGrado, William Frank; Moua, Shaker Ahmed; Sworin, Michael; Barrett, John Andrew; Edwards, David Scott; Harris, Thomas David; Rajopadhye, Milind; Liu, Shuang  
 PATENT ASSIGNEE(S): Du Pont Merck Pharmaceutical Co., USA  
 SOURCE: PCT Int. Appl., 459 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 6  
 PATENT INFORMATION:

18 ANSWER 20 OF 20 CAPLUS COPYRIGHT 2002 ACS (Continued)  
 study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
 (prepn. of radiolabeled platelet GPIIb/IIIa receptor antagonists as imaging agents for the diagnosis of thromboembolic disorders)  
 RN 167214-98-4 CAPLUS  
 CN Cyclo[3-(aminomethyl)-5-[[6-[[[6-hydrazino-3-pyridinyl]carbonyl]amino]-1-oxohexyl]amino]benzoyl-D-valyl-L-methyl-L-arginylglycyl-L-.alpha.-aspartyl] (9CI) (CA INDEX NAME)

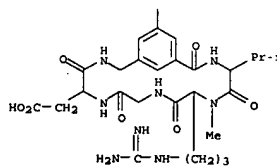
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WO 9422494	A1	19941013	WO 1994-US3256	19940329
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RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
US 5879657	A	19990309	US 1994-218861	19940328
AU 9465248	A1	19941024	AU 1994-65248	19940329
EP 692982	A1	19960124	EP 1994-912870	19940329
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BR 9406055	A	19960910	BR 1994-6055	19940329
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JP 08509710	T2	19961015	JP 1994-522205	19940329
JP 9042887	B2	20000522		
RO 114895	B1	19990830	RO 1995-1701	19940329
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FI 9504655	A	19951102	FI 1995-4655	19950929
NO 9503886	A	19951130	NO 1995-3886	19950929
PRIORITY APPLN. INFO.: US 1993-40336 A 19930330				
US 1994-218861 A 19940328				
WO 1994-US3256 W 19940329				

OTHER SOURCE(S): MARPAT 123:199405  
 AB Reagents for prepg. radiopharmaceuticals (QLGX)dX, QeLGX [d = 1-3; e = 2-20; LG = linking group; X = metal chelator; Q = Q1; R31 = (substituted) satd., partially satd., or arom. carbocyclyl, heterocyclyl, optionally bonded to LG; R32 = CO, CS, SO2, P(=Z)(ZR13); Z = S, O; m, n = 0-2; R1, R22 = H, (substituted) alkyl, alkenyl, alkynyl, cycloalkyl, aryl, heterocyclyl, -O, F, Cl, Br, iodo, CF3, cyano, bond to LG, etc.; R1R21, R22R23 = atoms to form a (substituted) 3-7 membered carbocyclyl; R1R2 = atoms to form a (substituted) 5-8 membered ring; R21, R23 = H, (halo)alkyl, PhCH2, R13 = H, alkyl, cycloalkyl, alkylcycloalkyl, aryl, alkylaryl, alkoxyalkyl; R2 = H, alkyl; J = -beta.-Ala, defined -alpha.-amino acid residue; K, M = defined -alpha.-amino acid residue; L = Y(CH2)vCO; Y = imino, O, S; v = 1,2, and the pharmaceuticals themselves, were prepd. Thus, title compd. (I) [prepn. given] was used at 1 mCi/kg i.v. for imaging jugular thrombi in dogs.  
 IT 167214-98-4DP, technetium-99m complex  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological)



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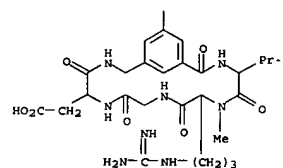
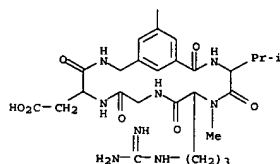
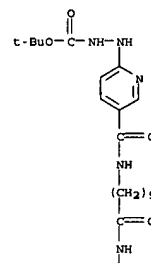
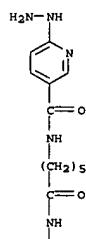


IT 167214-98-4P 167215-94-3P 167356-24-3P  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
 (prepn. of radiolabeled platelet GPIIb/IIIa receptor antagonists as imaging agents for the diagnosis of thromboembolic disorders)  
 RN 167214-98-4 CAPLUS

L8 ANSWER 20 OF 20 CAPLUS COPYRIGHT 2002 ACS (Continued)

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CM 2

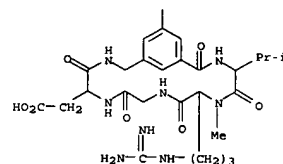
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CMF C2 H F3 O2

L8 ANSWER 20 OF 20 CAPLUS COPYRIGHT 2002 ACS (Continued)



L8 ANSWER 20 OF 20 CAPLUS COPYRIGHT 2002 ACS (Continued)



CM 1

CRN 167214-98-4  
CMF C38 H55 N13 O9

CM 2

CRN 76-05-1

CMF C2 H F3 O2

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